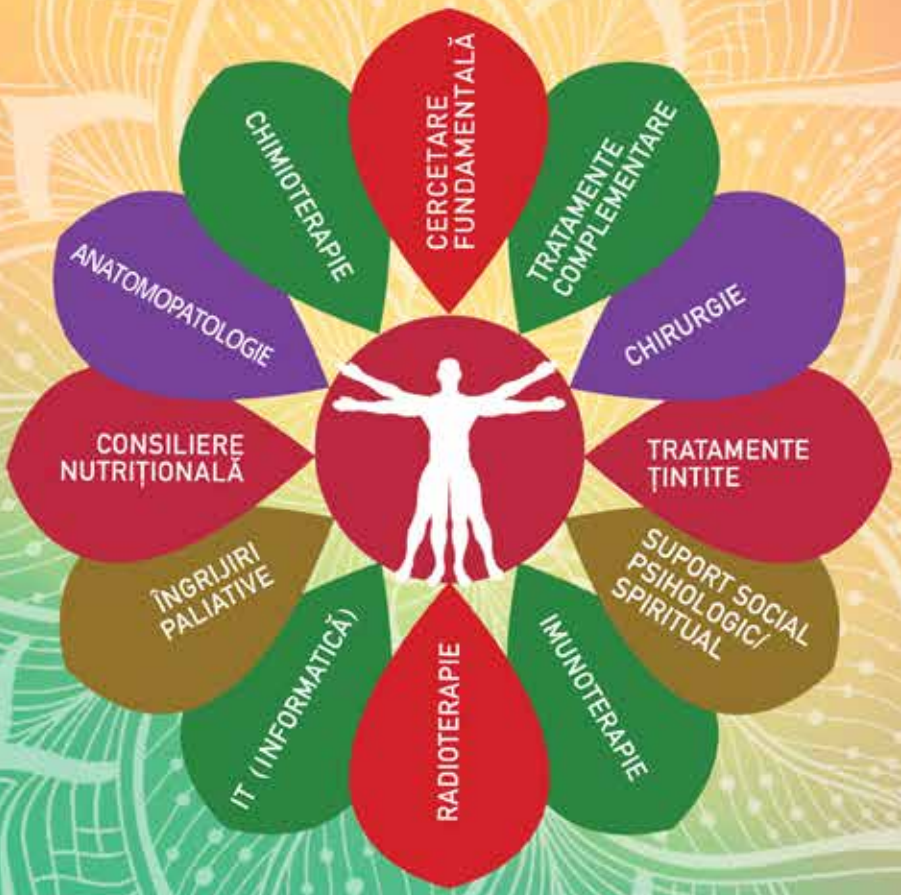
Al 4-lea Simpozion de Oncologie Translațională Personalizată pentru combaterea cancerului

SIMPOZION VIRTUAL

2020



STOP CANCER

Zilele de desfășurare:

17 septembrie · 24 septembrie · 1 octombrie
8 octombrie · 5 noiembrie · 12 noiembrie
3 decembrie · 10 decembrie · 17 decembrie

contact@stop-cancer-romania.ro

www.stop-cancer-romania.ro

Dragi colegi,

Anul acesta omenirea se confruntă cu pandemia Covid19 care ne-a schimbat tuturor viețile într-un mod radical. Pe parcursul pandemiei este esențială atenția acordată pacientilor cu cancer si personalizarea tratamentelor oncologice care trebuie sa ia in considerare, alaturi de alte comorbiditati, si riscul infectiei cu virusul SARS-Cov2. Pentru detalii va invitam sa consultati cu titlu informativ recomandarile ghidului ESMO: https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic.

În numele Comitetului de Organizare ne revine o desebită plăcere de a vă invita sa participati la sesiunile celui de-al patrulea Simpozion Translațional de Oncologie Personalizată pentru Combaterea Cancerului care se va desfasura virtual, pe platforma zoom, in perioada 17 septembrie-17decembrie 2020.

Simpozionul Translațional de Oncologie Personalizată (STOP Cancer-România) se desfășoară sub egida "Societatii Transdisciplinare de Oncologie Personalizată pentru Combaterea Cancerului" cu colaborarea "Societătii Nationale de oncologie medicala din România (SNOMR)", si a "Societatii Romane de Radioterapie si Oncologie Medicale" (SRROM).

La această a patra ediție participă chirurgi-oncologi, radioterapeuți, oncologi medicali, anatomopatologi, și cercetători în domeniul științelor fundamentale din țară, din Statele Unite ale Americii si din Europa. Intenția noastră este pe de o parte de a facilita dialogul între specialiștii oncologi din România și diaspora, iar pe de altă parte de a crea o platformă de oncologie translațională pentru schimbul de informații și idei între cercetătorii din diferite domenii ale științelor fundamentale și clinicienii oncologi în scopul dezvoltării de proiecte comune.

In premieră, in luna Decembrie 2020, vom avea o sesiune dedicată tinerilor oncologi la care vor prezenta lucrări si doua bursiere, sponsorizate de "Societatea Transdisciplinară de Oncologie Personalizată pentru Combaterea Cancerului" pentru studii in două laboratoare de cercetare din cadrul Facultații Weill Cornell din New York. Inițiativa de sponsorizare a tinerilor cercetatori romani in SUA continuă. Detalii vor fi postate in cursul lunii Ianuarie 2021 pe site-ul: http://www.stop-cancer-romania.ro

Sperăm ca această platformă de colaborare să îmbunătățească atât modalitățile de diagnostic ale cancerului cât și prognosticul și calitatea vieții pentru pacienții cu cancer din România.

Prezenţa lectorilor de peste hotare precum şi a dumneavoastră ne onorează şi garantează succesul Simpozionului. Limba oficială a Simpozionului este limba română.

Prezentările de la simpozion vor fi postate pe site-ul:

http://www.stop-cancer-romania.ro

Simpozionul va fi creditat cu 26 credite EMC!

Bine ați venit!

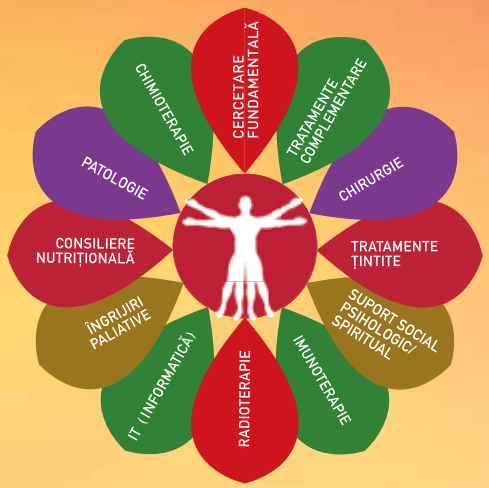
Comitetul de organizare:

DIRECTORI SIMPOZION:

Conf. Dr. Adina Croitoru, Prof. Asociat Dr. Doru Paul

ORGANIZATORI:

Dr. Vlad Croitoru, Dr. Florin Bacanu, Sef Lucrari Dr. Alina Musetescu



STOP CANCER

STOP CANCER ROMÂNIA
SIMPOZION VIRTUAL STOP CANCER 2020

17 Septembrie 2020

15:30-19:05 ROLUL ANATOMOPATOLOGULUI IN PRACTICA ONCOLOGICA MODERNA
Moderatori: DORU PAUL, ADINA CROITORU, GABRIEL BECHEANU, RAZVAN LAPADAT

15:30-15:50 CONF. DR. ADINA CROITORU, PROF. ASOCIAT DR. DORU PAUL,
"Oncologia in timpul pandemiei COVID-19"

15:50-16:30 PROF. DR. DAVID LYDEN (Weill Cornell Medical College, New York, SUA),
"Exosome biomarkers for early cancer detection" KEYNOTE SPEAKER

16:30-17:00 PROF. ASOCIAT DR. DORU PAUL (Weill Cornell Medical College, New York, SUA),
DR. RAZVAN CIPRIAN LĂPĂDAT (Anatomic Pathology and Cytopathology, Chicago, SUA),
"Molecular Tumor Board"

17:00-17:30 PROF. DR. ȘTEFAN N. CONSTANTINESCU (Université catholique de Louvain – De Duve Institute, Ludwig Institute for Cancer Research, Brussels, Belgia),
" Mutations versus Epigenetic Changes in Hematological and Solid Cancers"

17:30-17:40 PAUZA

17:40-18:15 Roche | Foundation Medicine "Tissue journey to diagnostic"

17:40-18:00 CONF. DR. GABRIEL BECHEANU (Institutul Clinic Fundeni, UMF Carol Davila),
"Quality in preanalitic"
18:00-18:15 DR. NICOLETA ANTONE (Institutul oncologic Cluj Napoca),
"Foundation Medicine - Testare Genomica Comprehensiva"

18:15-18:35 DR. GABRIELA OPREA (Personal Genetics),
"Perspectivele NGS in oncologie"

18:35-18:55 CONF. DR. VLAD HERLEA (Institutul Clinic Fundeni, Universitatea Titu Maiorescu, Bucuresti),
"Cresterea rolului anatomopatologului in sedintele multidisciplinare oncologice din spitale"

18:55-19:05 Q&A, Concluzii

24 Septembrie 2020

16:00-19:40 CANCER DE SAN
MODERATORI: DORU PAUL, ADINA CROITORU, SERBAN-DAN COSTA, GABRIELA OPREA-ILIES

16:00-16:30 PROF. DR. SERBAN-DAN COSTA (Universitäts Frauenklinik, Magdeburg, Germany),
"Tratamentul cancerului de san in perioada pandemiei"

16:30-17:00 PROF. DR. ALEXANDRU BLIDARU (IOB Al Trestioreanu, UMF Carol Davila, Bucuresti),
"Margini de rezectie in chirurgia cancerului mamar"
Autori: Alexandru Blidaru, Aniela Noditi, Cristian Bordea

17:00-17:20 Simpozion Novartis
DR. DRAGOS MEDIAN (Spitalul Clinic Filantropia, București),
"Kisqali - Redefinirea eficacitatii in cancerul de san metastatic"

17:20-17:50 Simpozion Roche
DR. LARISA CIULE (Institutul Oncologic Cluj-Napoca),
"Algoritmul optim de tratament in cancerul mamar HER2 pozitiv non-metastatic"

17:50-18:00 PAUZA

18:00-18:30 PROF. ASOCIAT DR. GABRIELA OPREA ILIES (Emory University School of Medicine, Atlanta, SUA),
"Molecular pathology of triple negative breast cancer"

18:30-18:50 DR. SIMONA VOLOVAT (UMF Grigore T. Popa, Institutul regional de oncologie, Iasi),
"Testele genomice in neoplasmul mamar, rol in preclinic si recomandari in clinica"

18:50-19:10 DR. MIHAI MARINCA (Institutul Regional de Oncologie, UMF "Gr T Popa", Iasi),
"Optiuni terapeutice in cancerul mamar triplu negativ"

19:10-19:30 DR. GABI RICU (Spitalul Militar Central, Bucuresti),
"Controverse in tratamentul radiologic al cancerului mamar localizat"

19:30-19:40 Q&A, Concluzii

1 Octombrie 2020

116:00-19:40 CANCERE GINECOLOGICE, CANCER PANCREATIC

16:00-18:00 CANCERE GINECOLOGICE
MODERATORI: ADINA CROITORU, DORU PAUL, DANIELA MATEI, DANA STANCULEANU

16:00-16:45 PROF. DR. DANIELA MATEI (Northwestern Medine, Feinberg School of Medicine, Chicago, SUA) KEYNOTE SPEAKER,
"Ovarian Cancer Stem Cells: From Hype to Hope"

16:45-17:05 CONF. DR. DANA STANCULEANU (IOB, UMF Carol Davila, Bucuresti),
"Tratamentul neoadjuvant ca prim gest terapeutic" SAU

17:05-17:25 DR. NICU BACALBASA (Institutul Clinic Fundeni, Bucuresti)
"Debulkingul ca prim gest terapeutic in neoplasmul ovarian stadiu III si IV?"

17:25-17:40 Simpozion Astra Zeneca
CONF.DR SERBAN NEGRU (Centrul de oncologie OncoHelp, UMF "Victor Babeș" Timișoara),TBA

17:40-18:00 Q&A, Concluzii

18:00-18:10 PAUZA

18:10-19:40 CANCERE PANCREATICE
MODERATORI: GABI CHIOREAN, ADINA CROITORU, DORU PAUL

18:10-18:40 PROF. DR. E. GABRIELA CHIOREAN (University of Washington, Seattle si Fred Hutchinson Cancer Research Center, SUA),
"Tinte moleculare in cancerul pancreatic"

18:40-19:00 DR RAZVAN IACOB (Institutul Clinic Fundeni, UMF Carol Davila, Bucuresti),
"Echoendoscopic guided fine needle aspiration for molecular characterization of borderline and non-resectable pancreatic ductal adenocarcinoma"
Autori: Iacob R, Bunduc S, Stoica B, Sorop A, Manea I, Constantinescu D, Moise E, Dima L, Sirbu M, Pantazica A.M, Ghionescu A, Chelaru R, Becheanu G, Dumbrava M, Croitoru A, Dima S, Popescu I, Gheorghe C

19:00-19:30 Simpozion Ipsen
DR. EVA SEDLACKOVA, MBA (First Faculty of Medicine, Charles University and General University Hospital),
"Treatment with somatostatin analogues in neuroendocrine tumors"

19:30-19:50 DR.TRAIAN DUMITRASCU (Institutul Clinic Fundeni, UMF Carol Davila Bucuresti),
"Rolul chirurgiei in adenocarcinomul ductal pancreatic"

19:50-20:00 Q&A, Concluzii

8 Octombrie 2020

16:00-19:40 CANCERE HEPATICE
MODERATORI: ALINA MIHAI, ADINA CROITORU, IRINEL POPESCU, DORU PAUL

16:00-16:30 PROF. DR. IRINEL POPESCU (Institutul Clinic Fundeni, Universitatea de medicina "Titu Maiorescu", Bucuresti),
"Tratamentul multimodal in hepatocarcinoame"

16:30-17:00 PROF. DR. ALINA MIHAI (Beacon Hospital-University College Dublin, Medisprof Cancer Center Cluj-Napoca),
"Rolul radioterapiei ablative stereotaxice in tumorile hepatice"

17:00-17:40 PROF. ASISTENT DR. ELIZABETA POPA (Weill Cornell Medical College, New York, SUA),
"Cholangiocarcinoma"

17:40-18:00 PROF. DR. IOANA LUPESCU (Institutul Clinic Fundeni, UMF Carol Davila, Bucuresti),
"Rolul Imagisticii sectionale in diagnosticul tumorilor cailor biliare"

18:00-18:10 PAUZA

18:10-18:40 PROF. ASOCIAT DR. DAN DUDA (Harvard Medical School, SUA)
"Rapidly evolving therapies in liver cancers"

18:40-19:00 Simpozion Bayer
DR STEFAN CURESCU (Spital Municipal Timisoara),
"Tratamentul secvențial Nexavar – "Stivarga în carcinomul hepatocelular avansat"

19:00-19:20 Simpozion Roche
CONF. DR. ADINA CROITORU (Institutul Clinic Fundeni, UM Titu Maiorescu, Bucuresti),
"Atezolizumab – breakthrough therapy for patients with hepatocarcinoma"

19:20-19:50 Simpozion Lilly
CONF.DR SERBAN NEGRU (Centrul de oncologie Onco Help, UMF "Victor Babeș" Timișoara), CONF DR MIKE SHENKER (UM CRAIOVA),
"Cyramza – vreau sa descopar si mai mult!"

19:30-19:40 Q&A, Concluzii

5 Noiembrie 2020

16:00-19:50 CANCER BRONHOPULMONAR
MODERATORI: ANCA-LIGIA GROSU, ADINA CROITORU, DORU PAUL, TUDOR CIULEANU

16:00-16:20 PROF. ASOCIAT DR. GABRIELA OPREA ILIES (Emory University School of Medicine, Atlanta, SUA),
“Molecular pathology in lung cancer”

16:20-17:50 PROF. DR. HORIA SARBU (Departamentul de chirurgie toracica Universitatea Erlangen, Germania),
“Tratamentul chirurgical in CBP”

16:50-17:10 PROF. DR. LUCIAN MIRON (Institutul Regional de Oncologie, UMF ”Gr T Popa”, Iasi),
“Cancerul bronho-pulmonar microcelular-imunoterapia, spre noi optiuni terapeutice!”

17:10-17:30 DR. MIRCEA DEDIU (Sanador, BucurestI),
”Current trends in the treatment of ALK positive NSCLC”

17:30-18:00 PROF. DR. ANCA-LIGIA GROSU (Department of Radiation Oncology, Medical Center, Medical Faculty, University of Freiburg, Freiburg, Germany),
”Lung cancer SBRT”

18:00-18:10 PAUZA

18:10-18:40 Simpozion Roche
DR. FILIPPO DE MARINIS, MD, PhD (European Institute of Oncology, Milan, Italy),
”Tecentriq role in lung cancer landscape”

18:40-19:00 PROF. DR. IONESCU DIANA (University of British Columbia , Vancouver, Canada, consultant BC Cancer Agency),
”Molecular Pathology of Lung Cancer”

19:00-19:30 Simpozion AstraZeneca
PROF. DR. MAZILU LAURA (Spitalul Judetetean Constanta, Universitatea Ovidius, Constanta):TBA

19:30-19:50 Simpozion BMS
DR. IORGA POLIXENIA (Spitalul Municipal Bucuresti):TBA

19:50- 20:20 PROF. DR. CIULEANU TUDOR (Institutul Oncologic Cluj Napoca, UM Iuliu Hatieganu, Cluj-Napoca),
”Cancerul Bronhopulmonar Nonmicrocelular”

20:20-20:30 Q&A, Concluzii

12 Noiembrie 2020

16:00-20:00 TUMORI SNC, SARCOAME

16:00-18:10 Tumori SNC
MODERATORI: DANIELA BOTA, ADINA CROITORU, DORU PAUL, HORIA VULPE

16:00-16:30 PROF. ASISTENT DR. IRINA MATEI (Weill Cornell Medical College, New York, SUA),
" Tumor exosomal CEMIP as a functional determinant, biomarker and therapeutic target in brain metastasis"

16:30-17:10 PROF. DR. DANIELA BOTA (University of California, Irvine, SUA),
"Cercetare in tumorile cerebrale"

17:10-17:40 PROF. ASISTENT DR. HORIA VULPE (Columbia University, New York, SUA),
"Interplay between immunotherapy and Radio surgery"

17:40-18:00 DR. RENATA ZAHU, PROF. DR. GABI KACSO (Clinica Amethyst, Cluj Napoca, UM Iuliu Hatieganu Cluj-Napoca),
"SBRT in metastazele cerebrale"

18:00-18:10 Q&A, Concluzii

18:10-18:20 PAUZA

18:20-20:00 Sarcoame
MODERATORI: GABRIELA GHEORGHE, ADINA CROITORU, DORU PAUL, GABI KACSO

18:20-18:50 PROF. ASOCIAT DR. GABRIELA GHEORGHE (Childrens Minnesota Pathology, Chicago, SUA),
"Diagnostic diferential: limfom, sarcom, carcinom"

18:50-19:10 DR. BOGDAN MOLDOVAN (Spital Sf Constantin, Brasov),
"Abordarea multidisciplinara a sarcoamelor în experienta Spitalului Sf Constantin Brasov de la ILP la protezele custom"

19:10-19:30 CONF. DR. LAURENTIA GALES (IOB, Al Trestioreanu, UMF Carol Davila),
"Algoritm de selectie a tratamentului in sarcoame"

19:30-19:50 PROF. DR. GABI KACSO (Clinica Ametist Cluj Napoca, UM Iuliu Hatieganu, Cluj Napoca),
"Update in radioterapia sarcoamelor"

19:50-20:00 Q&A, Concluzii

3 Decembrie 2020

16:00-19:20 CERCETARE TRANSLATIONALA

MODERATORI: DORU PAUL, ADINA CROITORU, MIRCEA IVAN, DAN DUDA

16:00-16:40 DR. RADU MINEA (Neurological Surgery, USC University of Southern California, Los Angeles, SUA),
"Modulating the Innate Immune Responses of Immunologically Cold Tumors with Targeted Radionuclides"

16:40-17:20 CSI DR. SIMONA DIMA (Institutul Clinic Fundeni, CEMT, Bucuresti)
"Cercetare"

17:20-17:40 TBA

17:40-17:50 PAUZA

17:50-18:30 PROF. ASOCIAT DR. DAN DUDA (Harvard Medical School, SUA),
"Revisiting the century-old "Seed and Soil" theory on tumor metastasis"

18:30-18:50 Simpozion Roche
Conf. Dr. Adina Croitoru (Institutul Clinic Fundeni,UM Titu Maiorescu, Bucuresti),
" Personalised Medicine: Marking A New Era In Cancer Patient Management"

18:50-19:10 SIMPOZION BMS
CONF. DR. LAURENTIA GALES (IOB, Al Trestioreanu, UMF Carol Davila)

19:10-19:20 Q&A, Concluzii

10 Decembrie 2020

16:00-19:40 MELANOM MALIGN
MODERATORI: ROXANA DRONCA, ADINA CROITORU, DORU PAUL, GEORGE CALIN

16:00-16:30 PROF. DR. SABINA ZURAC (Spitalul Clinic Colentina, UMF Carol Davila, Bucuresti),
”Probleme de diagnostic in melanomul malign-Consensul European 2019”

16:30-17:10 PROF. ASOCIAT DR. ROXANA DRONCA (Mayo Clinic, SUA),
”Cercetare in Melanomul malign”

17:10-17:40 PROF. DR. ALEXANDRU BLIDARU (IOB Al Trestioreanu, UMF Carol Davila, Bucuresti),
”Biopsia ganglionului santinela in melanomul malign cutanat”
Autori: Alexandru Blidaru, Silviu Voinea, Cristian Bordea

17:40-18:00 DR. DAN JINGA (Clinica Neolife),
”Melanomul malign st II si III, tratament adjuvant”

18:00-18:10 PAUZA

18:10-18:30 Simpozion Novartis
DR. LARISA CIULE (Institutul Oncologic Cluj-Napoca),
”Melanom – Consideratii practice in melanomul avansat”

18:30-18:50 Simpozion BMS
DR. RAZVAN CURCA (Spitalul municipal Alba Iulia),
”Imunoterapia combinata si a terapiei tintite in melanomul avansat ”

18:50-19:30 PROF. DR. GEORGE CĂLIN (MD Anderson, Houston, SUA)
”Small RNAs with big impact”

19:30-19:50 Simpozion Merck
DR. ZOB DANIELA (IOB “Al Trestioreanu”, Bucuresti),
”Carcinomul Merkel”

19:50-20:00 Simpozion Sanofi
TBD (Carcinom scuamos)

19:30-19:40 Q&A, Concluzii

17 Decembrie 2020

16:00-19:50 TINERI DOCTORI CARE NU VOR SA PARASEASCA ROMANIA
MODERATORI: ADINA CROITORU, DORU PAUL, CRISTI LUNGULESCU, IRINA CAZACU

16:00-16:15 DR. CRISTI LUNGULESCU

16:15-16:30 DR. IRINA CAZACU

16:30-16:45 DR. MONICA MIRON

16:45-17:00 DR. VLAD CROITORU

17:00-17:15 LAURA PATRAS (PhD studiu post-doc),
”Exosomii in laboratorul Prof Leyden”

17:15-17:30 LEONA CHITOIU (studenta bioinformatica)

17:30-17:45 DR. SIMONA VOLOVAT

17:45-18:00 DR. PETRA CURESCU

18:00-18:10 PAUZA

18:00-18:20 Simpozion Roche
DR. IOANA LUCA (Institutul Clinic Fundeni),
„Sharing clinical experience with Tecentriq in urotelial cancer patients”

18:30-18:40 TBA

18:40-18:55 DR. ADELINA GHEORGHE

18:55-19:10 DR. ANDRA VISAN (Spital Sanador)

19:10-19:25 DR. STEFAN

19:25-19:40 rezident Serban Negru.

19:40-19:55 DR.

19:55-20:05 Q&A, Concluzii

COMITET STIINTIFIC:

Dr. Florin Achim
Prof. Dr. Carmen Ardelean
Dr. Florin Băcanu
Dr. Rodica Birla
Dr. Florentina Bratu
Dr. Dorin Bica
Prof. Dr. Daniela Bota
Prof. Dr. Robert Bota
Dr. Florina Buica
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Prof. Asist. Dr. Gabriela Gheorghe
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Prof. Asist. Dr. Daniela Matei
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Dr. Ovidiu Palea
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Prof. Dr. Adrian Salic
PhD. Livia Sima
Sef Lucr. Dr. Michael Schenker
Dr. Alina Sturdza
PhD. Nikos Tsoulos
Dr. Nina Tunariu
Dr. Adrian Udrea
Dr Adrian Ungureanu
Dr. Mihaela Vlad
Prof. Asist. Dr. Horia Vulpe

1.The systemic hallmarks of cancer

Doru Paul:Weill Cornell Medical College, New York, SUA

Cancer cells and cancer tissues communicate between themselves and with the rest of the organism through complex networks that allows cancer to invade and spread systemically. Cancer is a multi-layered disease that involves the whole organism and we believe that, in order to better understand the metastatic process, there is an urgent need to zoom-out from the cellular and the stromal view and broaden our perspective by including the organismic level.

In the presentation, we introduce the cancer system concept, describe the outstanding systemic hallmarks of cancer and discuss several new therapeutic approaches that can be developed using this evolving paradigm.

2.The Gene Master Regulators of tissues and cells collected from patients with blood, lung, kidney, prostate or thyroid cancer

Dumitru Iacobas: Personalized Genomics Laboratory, Prairie View A&M University Texas, SUA

Most cancers occur from nowhere, without being inherited or directly caused by a steady deficient diet (affecting the microbiome), exposure to radiation or carcinogenic toxins, or bad habit (like smoking), although such risk factors increase the chances of the “bad luck”.
Tumors are heterogeneous, composed of regions with distinct characteristics, some of them malignant, some others preserving the normal features of the tissue. In spite of a very rich literature, there is not yet a comprehensive explanation of cancer development, nor a perfect therapeutic solution. Moreover, with all similarities, each human is unique and has a unique lifeline, so, although a trained pathologist can recognize the cancer type, the tumors are not identical, nor develop identically or respond identically to treatment. Therefore, instead of targeting the same alleged gene biomarker for all humans with a particular cancer form, we devised a method by which the cancer of the actual patient itself indicates us what genes are now commanding it. We call these commanders “gene master regulators” (GMRs) and identify them by profiling the gene expression in tumor biopsies or blood samples (pending on the suspected cancer type) using RNA sequencing or microarray platforms. Here, we prove that cancer nuclei and surrounding normal tissue are governed by distinct GMRs and that smart manipulation of a GMR’s expression selectively affects cancer cells. The method, consistent with our Genomic Fabric Paradigm, relies on an original mathematical algorithm that establishes the gene hierarchy from the transcriptomic profiles of tumor biopsies based on their Gene Commanding Height (GCH). GCH is a composite measure of gene expression control and coordination with major functional pathways. We present validation of the approach using microarray data obtained in our previous NYMC laboratory by profiling human kidney, thyroid, blood, lung and prostate cancer samples. The GMR approach provides the most legitimate targets for cancer gene therapy. It is also personalized and time-sensitive because the GMR hierarchy is unique for each patients and changes slowly during cancer development.

3.Role of tissue transglutaminase in anti-tumor immunity

Livia E. Sima[1#], Horacio Cardenas[1], Siqi Chen[2], Yinu Wang[1], Hao Huang[1], Guanyuan Zhao[1], Bin Zhang[2], Daniela Matei[1]

[1] Department of Obstetrics and Gynecology, Feinberg School of Medicine, Northwestern University, Chicago, IL, 60611, USA

[2] Department of Medicine-Division of Hematology/Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, 60611, USA

[#]Current affiliation: Department of Molecular Cell Biology, Institute of Biochemistry of the Romanian Academy, Bucharest,

Romania

Tissue transglutaminase (TG2), an enzyme that catalyzes transfer of acyl groups between glutamine and lysine residues, is overexpressed in cancer and is involved in resistance to chemotherapy, metastasis, and cancer stem cell signaling. Our group demonstrated that TG2 knock-down prevented metastasis in intraperitoneal (ip) and orthotopic ovarian cancer xenograft models. While the functions of TG2 in cancer cell lines have been well characterized, little is known about the role of TG2 in the host in cancer models. We hypothesized that TG2 knock-out ($TG2^{-/-}$) in the host will alter OC tumor progression. We used murine ID8 ovarian cancer cells injected ip into wild-type (WT) and $TG2^{-/-}$ mice, and investigated tumor progression and anti-tumor immune response by analyzing the major immune cell subsets in spleens and ascites from tumor-bearing animals.

We observed a significant decrease in tumor burden in $TG2^{-/-}$ *vs.* WT mice as evidenced by less ascites accumulation (1.712 *vs.* 4.202 mL, $p = 0.0134$, $n = 23$), increased median survival (46 *vs.* 43 days, $p = 0.020$, $n = 12$), and decreased number of cancer cells in ascites (23.33×10^6 *vs*. 77.38×10^6, $p = 0.018$, $n = 5$). This phenotype was accompanied by significant changes in anti-tumor immunity. $CD8^+$ cells recovered from ascites or spleens of $TG2^{-/-}$ mice expressed higher levels of PD-1. *Ex vivo* stimulation of T cells from ascites revealed a significant increase in responsive IFNγ-secreting $CD8^+$ and $CD4^+$ cells in $TG2^{-/-}$ compared with WT mice ascites. Interestingly, $TG2^{-/-}$ mice ascites contained an increased number of effector/memory $CD8^+$ T cells over the naïve and central memory phenotypes, suggesting that TG2 may play a role in T cell differentiation during anti-tumor response. Concomitantly, we found an increase of pStat3 levels in $TG2^{-/-}$ memory $CD8^+$ T cells *in vivo* and upon *in vitro* activation. On the other hand, decreased accumulation of myeloid cells occurred in ascites of $TG2^{-/-}$ mice. Expression of PD-L1 was decreased on all myeloid subsets as well as on $EpCAM^+$ cells in $TG2^{-/-}$ ascites, indicating that the tumor microenvironment is less immunosuppressive in the absence of TG2. ID8 cells treated with $TG2^{-/-}$ mice ascites generated fewer colony-forming units ($p = 0.0052$) than ID8 cells treated with WT mice ascites. Depletion of $CD8^+$ T cells using anti-CD8 antibodies produced an increase in ascites volume in $TG2^{-/-}$ mice, reverting the phenotype towards that of isotype-treated WT animals.

Collectively, our data suggest decreased tumor burden concurrently with increased activation and effector functions of T cells, and loss of immunosuppressive signals in the tumor microenvironment resulting in development of an anti-tumorigenic phenotype in $TG2^{-/-}$ mice.

Keywords: ovarian cancer, tissue transglutaminase, immune cells, $CD8^+$ T cells, myeloid cells, ID8 cells, tumor microenvironment

Rolul transglutaminazei in imunitatea anti-tumorala

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Transglutaminaza tisulara (TG2), o enzima care catalizeaza transferul de grupari acil intre resturile de glutamina si lizina, este supraexprimata in cancer si este implicata in rezistenta la chemoterapie, in metastaza si in semnalizarea celulelor stem canceroase. Grupul nostru a demonstrat anterior ca silentierea TG2 previne metastazarea atat in modele intraperitoneale (ip) cat si in xenografe ortotopice de cancer ovarian. In timp ce functiile TG2 in celulele canceroase au fost bine caracterizate, nu se cunosc prea multe despre rolul TG2 in organismul gazda in modele de cancer. Am pornit de la ipoteza ca eliminarea genetica a TG2 (TG2-/-) in gazda va modifica progresia tumorala. Am utilizat celule murine de cancer ovarian ID8 injectate ip in soareci de tip salbatic (wild-type, WT) si knock-out (TG2-/-) si am investigat progresia tumorala si raspunsul imun anti-tumoral prin analiza tipurilor majore de celule imune din splina si ascita colectata de la animalele purtatoare de tumori.

Am observat o scadere semnificativa a incarcarii tumorale in soarecii TG2-/- vs. WT care s-a manifestat printr-o acumulare

mai scazuta de ascita (1.712 vs. 4.202 mL, p = 0.0134, n = 23), cresterea duratei medii de viata (46 vs. 43 de zile, p = 0.020, n = 12) si scaderea numarului de celule tumorale in ascita (23.33 × 106 vs. 77.38 × 106, p = 0.018, n = 5). Acest fenotip a fost insotit de schimbari semnificative in imunitatea anti-tumorala. Celulele CD8+ din ascita si splinele soarecilor TG2-/- au exprimat nivele mai crescute ale PD-1. Stimularea lor ex vivo a dezvaluit o crestere a celulelor CD8+ si CD4+ care secreta IFNγ in soarecii TG2-/-. In mod remarcabil, ascita soarecilor TG2-/- a continut un numar crescut de celule T CD8+ de memorie efectoare comparativ cu celulele T de memorie centrale si cu cele naive, sugerand ca TG2 ar putea juca un rol in diferentierea celulelor T. Concomitent, am observat o crestere a nivelelor pStat3 in celulele T CD8+ de memorie TG2-/- in urma activarii in vitro. Pe de alta parte, am inregistrat o scadere a acumularii de celule mieloide in ascita soarecilor TG2-/-. Expresia PD-L1 a scazut atat la suprafata celulelor mieloide cat si a celulelor EpCAM+ in ascita TG2-/-, indicand faptul ca micromediul tumoral este mai putin imunosupresiv in absenta TG2. Celulele ID8 tratate cu ascita TG2-/- a generat mai putine unitati formatoare de colonii decat celulele tratate cu ascita WT. Depletia celulelor T CD8+ utilizand anticorpi anti-CD8 a produs o crestere a volumului de ascita in soarecii TG2-/- reversand fenotipul catre cel manifestat de cei WT tratati cu izotip.

Impreuna, datele noastre sugereaza o scadere a incarcarii tumorale concomitent cu cresterea activarii si functiei efector a celulelor T si pierderea semnalelor imunosupresive in micromediul tumoral rezultand in dezvoltarea unui fenotip anti-tumorigenic in soarecii $TG2^{-/-}$.

Cuvinte cheie: cancer ovarian, transglutaminaza tisulara, celule imune, celule T $CD8^{+}$, celule mieloide, celule ID8, micromediu tumoral.

4.Clinical significance of epithelial to mesenchymal transition molecular markers in pancreatic ductal adenocarcinoma

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Background: Epithelial to mesenchymal transition (EMT) is one of the key factors contributing to aggressiveness of pancreatic ductal adenocarcinoma by increasing metastatic potential. New therapies combining cytotoxic drug agents with EMT inhibition are currently emerging, thus the identification of PDAC cases with a distinct EMT profile is mandatory.

Methods: Thirty-five patients with resectable PDAC were included in the analysis. Quantitative gene expression has been conducted for transcription factors controlling EMT process - FOXA2, GATA6, SNAIL, SLUG, TWIST1, TWIST2, ZEB1. Relative gene expression has been quantified for each gene using tumor-non-tumor tissue pairs and beta-actin as housekeeping gene. The correlations of gene expression within the transcription factors network was investigated by analysis of covariance and correlations patterns were used in order to define key transcriptional profiles specific to the EMT process. Prognostic value for tumor recurrence and survival were assessed by Cox proportional hazards model. Recurrence free survival and overall survival were estimated by Kapan Meier method.

Results: Significant overexpression of EMT transcription factors was identified in, 82.3% of cases for Twist1, 48.5% SNAIL, 42.6% SLUG, 35.3% TWIST2, 32.3% ZEB1. Significant down regulation was registered in 64.7% of subjects for GATA6 and in 58.8% for FOXA2. Both SNAIL and SLUG were positively correlated with TWIST2 and ZEB1 (p=0.0027 and p=0.03, p=0.02 and p=0.02 respectively). Based on the correlation matrix there were 5 EMT profiles generated: FOXA2down/SNAILup, GATA6down/TWIST1up, GATA6down/ZEB1up, TWIST1up/SNAILup and and TWIST1up/ZEB1up. Multivariate survival analysis has indicated that all these profiles excepting GATA6down/TWIST1up are independent predictors for tumor recurrence and patient survival. According to Kaplan Meier survival analysis EMT profile characterized by GATA6 downregulation and ZEB1 overexpression has the worst prognosis, with 3 months' time to tumor recurrence and 9 months survival time (p=0.01 and p=0.008 respectively).

Conclusions. Our study has identified by relative gene expression quantification EMT profiles that independently predict both time to recurrence and survival in resectable PDAC patients. In our study group, cases defined by Gata6 downregulation/Zeb1 up-regulation had the worst prognosis.

5.Immunotherapy in prostate cancer

Daniel Danila: Memorial Sloan Kettering Cancer Centre, New York, SUA

Androgen deprivation therapy is the mainstay for men with metastatic prostate cancer, but typically the disease will inevitably progress into a castration-resistant (mCRPC) phenotype. Since 2005, many agents were shown to improve overall survival in mCRPC patients., including taxane-based chemotherapy, bone-targeting radium-223, androgen biosynthesis inhibitors and novel receptors antagonists. More headway has been made in molecularly targeted treatments such as PARP inhibitors for DNA-repair defective tumors, however, there is still an unsatisfied need for durable responses. The promise of immune-based therapies has shifted the oncological management. The infiltration of prostate cancer tissue by inflammatory cells and T cells suggests that this cancer is a target of a host immune response and thus, a potential candidate for immunotherapy. Sipuleucel-T is currently the only immunotherapy approved for the treatment of mCRPC, however, it does not affect PSA, or induce tumor regression, limiting Its clinical indications. The recent successes of immunotherapy checkpoint blockades with durable responses in patients with melanoma, lung cancer, kidney cancer, and ovarian cancer have yet to be reproduced in mCRPC. Monotherapy with ipilimumab, a cytotoxic T-lymphocyte antigen 4 (CTLA-4) inhibitor, has demonstrated modest clinical responses in mCRPC. Pembrolizumab, an Inhibitor of programmed cell death protein 1-receptor of lymphocytes, has been approved in all solid tumors with microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors, including mCRPC. Trials of PROSTVAC-VF, a Poxviral-based PSA-targeted vaccine, suggests an association with overall survival and are currently undergoing phase 3 testing for minimally symptomatic mCRPC. The oncologic care has significantly improved since better understanding of biology and with the refinement of our therapeutic tools. More research is needed to increase the clinical impact on patients with mCRPC.

6.Asocieri terapeutice în tratamentul metastazelor cerebrale ale melanomului malign, terapii moleculare țintite, imunoterapie și radioterapie

*Dan Jinga, Ana Bancila, Lucian Bratu: Centrul Medical Neolife, Bucuresti*Melanomul malign cutanat reprezinta a 3-a cauza de metastaze cerebrale in populatia cu tumori solide, dupa carcinomul pulmonar si cel mamar. Aparitia metastazelor cerebrale se coreleaza cu deficite neurologice importante si cu o speranta redusa de supravietuire, in medie de 3 luni pentru formele netratate si de 9 luni pentru cele tratate local si sistemic clasic.

Introducerea in ultimii ani, inclusiv in Romania, a tratamentelor locale moderne (radiochirurgia stereotactica) si a tratamentelor sistemice novatoare (imunoterapia si terapia tintita anti-BRAF) a permis imbunatatirea rezultatelor terapeutice.

Metoda: utilizand banca de date personale a pacientilor tratati in ultimii 15 ani am identificat 299 de cazuri de melanom malign cutanat (10,5% din numarul de pacienti); varsta medie in momentul diagnosticului a fost de 52 de ani, indicele Breslow mediu de 3.12 mm; intervalul liber de boala mediu a fost estimat la aproximativ 40 de luni, iar supravietuirea globala medie la 48 de luni. 13% dintre pacienti au prezentat metastaze cerebrale (39 de pacienti), fie in momentul diagnosticului (15 pacienti), fie in cursul evolutiei bolii de la stadiile I, II si III (18 pacienti); pentru 6 pacienti nu exista date privind stadiul initial al bolii.

Rezultate: comparativ cu populatia generala cu diagnostic de melanom malign cutanat (299 de pacienti), populatia cu melanom malign cu metastaze cerebrale (39 de pacienti) prezinta aceeasi varsta medie la debutul bolii, un Indice Breslow mediu semnificativ mai mare (4,74 mm versus 3,12 mm), cu un interval liber de boala mediu semnificativ mai mic (33 de luni versus 40 de luni); in ceea ce priveste supravietuirea globala medie, aceasta este semnificativ mai mica in cazul pacientilor cu stadiile IIIC si IV in momentul diagnosticului (22,6 luni comparativ cu 48 de luni). Tratamentul local al metastazelor cerebrale a fost chirurgical pentru 30% dintre pacienti si paliativ pentru 60% (iradiere cerebrala totala); pentru 10% dintre pacienti au fost administrate tehnici combinate de tratament local sau terapie de suport.

In ceea ce priveste tratamentul sistemic, 25% dintre pacientii cu metastaze cerebrale au primit terapii moderne (imunoterapie si terapie anti BRAF).

Concluzii: introducerea noilor tehnici de tratament local si sistemic a permis cresterea sperantei de viata a pacientilor cu melanom malign cutanat cu metastaze cerebrale; studiul prezinta principalele terapii utilizate in prezent, precum si asocierile acestora.

7.CX3CR1 identifies PD-1 therapy-responsive CD8 T cells that may mediate the response to combined chemo-immunotherapy for metastatic melanoma

Roxana Dronca: Mayo Clinic, Florida

Although immune checkpoint inhibitors have been reported to result in durable clinical benefit in a subset of patients with advanced cancer, primary or acquired resistance is common and is a pressing challenge in the management of these patients. Notably, once cancer patients whose tumors have progressed upon anti-PD-1 therapy have been found to benefit from the addition of salvage chemotherapy, even though cytotoxic chemotherapy is classically viewed as toxic to immune cells. However, the mechanism responsible for the successful clinical outcomes of chemo-immunotherapy is not completely understood. Here we show that a subset of $CD8^+$ T cells expressing the chemokine receptor CX3CR1 are able to withstand cytotoxic chemotherapy and significantly increased in patients with metastatic melanoma who responded to combined chemo-immunotherapy (paclitaxel and carboplatin with PD-1 blockade). The $CX3CR1^+CD8^+$ T cells have an effector memory phenotype and the ability to efflux chemotherapy drugs via the ABCB1 transporter. Our preclinical modes have also identified an optimal sequencing of chemo-immunotherapy that resulted in an increase of $CX3CR1^+CD8^+$ T cells.

8.Optical techniques for intraoperative guidance of cancer surgery

Laura Marcu: University of California, Davis

Abstract: Fluorescence measurements provide information about biochemical, functional and structural changes in fluorescent bio-molecular complexes in tissues and cells including structural proteins, enzyme metabolic co-factors, lipid components, and porphyrins. Typically, these changes are a result of either pathological transformation or therapeutic intervention. We investigate time-resolved fluorescence spectroscopy (TRFS) and fluorescence lifetime imaging microscopy (FLIM) techniques that utilize label-free fluorescence lifetime contrast to detect such changes in-vivo. This presentation will overview clinically-compatible TRFS and FLIM instrumentation and present studies that demonstrate the diagnostic potential of these optical techniques in neurosurgical procedures. We show that intrinsic fluorescence signals provide useful contrast for the intraoperative guidance of brain tumors surgical resection and delineation of radiation induced injury from tumor recurrence.

9.Phsician Burnoyut: Healing the Healer

Robert Bota: Department of Psychiatry and Human Behavior, University of California, Irvine, SUA

This is not a fair fight. Medical school and residency brainwashes you over 10 years. At that time we develop a set of habits' that in medical school and residency are very useful. However, postponing self-care, doing it all ourselves to make sure is "done right" and working with sick patients in bad affective states starts wearing on us.

Sir William Osler said "The practice of medicine will be very much as you make it – to one a worry, a care, a perpetual annoyance; to another, a daily job and a life of as much happiness and usefulness as can well fall to the lot of man", however, wishing burnout away is not working in this day and age.

The concept of burnout emerged 50 years ago to describe the clinic staff caring for vulnerable patients in free clinics. Since then, the term burnout has been used to describe job-related stress in health practice environment. Based on the foundational work of Maslach in 1980's researchers have described burnout as a combination of emotional exhaustion, depersonalization, and low sense of accomplishment. This is caused by the chronic stress of medical practice. Pragmatically, burnout is associated with more medical errors, decreased professional work effort, and lower patient satisfaction.

In this talk I will describe psychological mechanisms involved, and how to recognize and address burnout in ourselves and in our colleagues.

10.Stromal vulnerabilities in liver cancers

Dan G. Duda, DMD, PhD: Edwin L. Steele Laboratories for Tumor Biology, Massachusetts General Hospital Research Institute, Harvard Medical School

Surgical treatments offer the chance for cure in liver cancers such as hepatocellular carcinoma (HCC). However, many of the resected or transplanted patients experience disease progression. Moreover, many patients present with unresectable disease at diagnosis. In such cases, until recently, available treatment options – local and systemic – have been limited in efficacy which led to dismal survival rates in advanced HCC. But more recent developments in oncology have offered renewed hope for advanced HCC patients. Hypofractionated radiation has shown feasibility and promise in unresectable HCC setting, and is now being tested in a randomized phase III trial (clinicaltrials.gov identifier NCT03186898). Antiangiogenic agents have strongly impacted the management of advanced HCC, with multiple drug options in first line setting (sorafenib, lenvatinib) and second line setting (regorafenib, cabozantinib, ramucirumab). Notably, immunotherapy with anti-PD-1/PD-L1 antibodies has shown real potential to transform advanced HCC therapy, both in first line and second line settings. Finally, combinations of these new strategies are very attractive approaches, as they promise durable and profound responses in advanced HCC. But in order to achieve this promise, these concepts require greater understanding based on mechanistic preclinical studies and validation in correlative studies in clinical trials as a basis to establish optimal combinatorial strategies. I will present results from clinical correlative studies and preclinical models of these diseases performed at our institution and in collaboration with other American and European investigators. The insights gained from this “bench-to-the-bedside and back” approach raise the hope for a more efficient development of targeted agents in advanced, with the goal of increasing survival in patients afflicted with this aggressive and deadly disease.

Recommended reading:

1. Chen Y, Ramjiawan RR, Reiberger T, Ng MR, Hato T, Huang Y, Ochiai H, Kitahara S, Unan EC, Reddy TP, Fan C, Huang P, Bardeesy N, Zhu AX, Jain RK, Duda DG. CXCR4 inhibition in tumor microenvironment facilitates anti-PD-1 immunotherapy in sorafenib-treated HCC in mice. *Hepatology* 2015; 61: 1591-602.

2. Hato T, Zhu AX, Duda DG. Rationally combining anti-VEGF therapy with checkpoint inhibitors in hepatocellular carcinoma. *Immunotherapy* 2016; 8: 299-313.

3. Popp I, Niedermann G, Grosu AL, Duda DG. Immune modulation by hypofractionated stereotactic radiation therapy: Therapeutic implications. *Radiotherapy and Oncology* 2016; 120: 185-94.

4. Ramjiawan RR, Griffioen AW, Duda DG. Anti-angiogenesis for cancer revisited: Is there a role for combinations with immunotherapy? *Angiogenesis* 2017; 20: 185-204.

5. Grassberger C, Hong TS, Hato T, Yeap B, Wo J, Tracy M, Bortfeld T, Wolfgang J, Eyler C, Goyal L, Clark JW, Crane CH, Koay EJ, Cobbold M, DeLaney TF, Jain RK, Zhu AX, Duda DG. Differential Association between circulating lymphocyte populations with outcome of radiotherapy in subtypes of liver cancer. *International Journal of Radiation Oncology, Biology and Physics* 2018; 101: 1222-5.

11.Tumor Exosomes: From Mediators of Systemic Disease to Biomarkers of Metastatic Spread

Irina Matei: Weill Cornell Medical College, New York, SUA

Cancer is a systemic disease and metastasis to distant vital organs such as lung, liver, and brain is the most devastating feature of cancer progression, responsible for over 90% of cancer-associated deaths. Reciprocal interactions between tumor cells and their local and distal microenvironments as well as the immune system drive cancer progression and metastasis, immunosuppression and therapy resistance. Our investigation of the tumor-secreted factors that mediate the crosstalk between tumors and cells in the remote metastatic microenvironment has led to the discovery that tumor-secreted microvesicles, known as exosomes, alter the microenvironment at future sites of metastasis to form pre-metastatic niches, creating a favorable “soil” for incoming metastatic “seeds”. Unbiased proteomic profiling of exosomes revealed distinctive protein expression patterns, and analysis of plasma exosomes from cancer patients that later developed site-specific metastasis revealed that exosome protein content could predict metastatic spread to lung, liver, and brain. Importantly, exosomes have complex cargo, that in addition to proteins includes DNA, coding and non-coding RNAs, as well as lipids and metabolites, all of which have biomarker potential. Through application of novel technologies such as asymmetric flow field-flow fractionation to exosome research we have recently unraveled the heterogeneity of exosome populations, identifying two new distinct exosome subpopulations (large and small exosome vesicles) and demonstrating the existence of a population of novel, nanoparticles with distinct structure, composition and function termed “exomeres”. Undoubtedly, further insight into exosome biogenesis, molecular composition, biodistribution, and functions will open new avenues for translational studies of the diagnostic, prognostic, and therapeutic applications of extracellular vesicles/particles.

12.Tumor Biopsy: Are We Ready for the ‘Liquid’ Revolution?

Razvan Lapadat: Anatomic Pathology and Cytopathology

Oncology traditionally relied on morphologic examination of neoplastic tissues and individual cells as its main diagnostic instruments, while molecular biology joined the diagnostic armamentarium during the last two decades. Liquid biopsy represents a novel minimally invasive alternative to surgical biopsy for molecular markers in blood and other body fluids of cancer patients. It overcomes the hurdles in the clinical assessment of tumors derived due to lack of accessibility to the tumor tissue and its clonal heterogeneity. Additionally, body fluid molecular analysis reflects the genetic fingerprint of primary and metastatic lesions and provides real-time monitoring of tumor evolution, holding a great promise for personalized medicine. Past technical hurdles have been mitigated by newly developed techniques such as next-generation sequencing, expanding the clinical applications of liquid biopsy. Initially correlated to disease prognosis, liquid biopsy derived data are currently used for cancer diagnosis, most importantly for the prediction of response or resistance to therapy. Identification of specific mutations in target genes can aid in therapeutic decisions, both in the appropriateness of treatment and in the advanced identification of secondary resistance, aiming to early diagnose disease progression. This presentation will review classical cytology diagnostic methods followed by describing liquid biopsy aspects including tumor-derived exosomes, circulating tumor cells, tumor-educated platelets, and circulating tumor miRNAs and mRNAs.

13.CAR T cell therapy: the future is now

Doru Paul:Weill Cornell Medical College, New York, SUA

Genetically engineered chimeric antigen receptor (CAR) T cells are a new class of therapeutic agents, truly, “live drugs”, that has been associated with significant and durable responses in refractory cases of several types of hematological malignancies. The chimeric antigen receptor (CAR) is created in the laboratory by genetic engineering and is designed to bind to certain proteins present on the surface of cancer cells. The CARs are transfected to the patients’ T lymphocytes. Subsequently, the T cells are grown in large numbers and then reinfused to the patient. Once infused, CAR T cells specifically find and kill the cancer cells that have the specific protein that the receptor is designed to bind. Each CAR T cell can kill many tumor cells. Also, CAR T cells may promote immune surveillance to prevent tumor recurrence through antigen release at the time of destroying the cancer cells, by assisting other tumor-infiltrating lymphocytes to attack tumors, or by their own persistence in the circulation. CD19 CAR T therapy has been the most successful CAR T therapy used so far. In acute lymphoblastic leukemia (ALL), CD19 CAR T cell treatment, has been associated with durable responses in approximately two thirds of the patients, while in diffuse large B cell lymphomas (DLBCL), CD19 CAR T cell therapy lead to 30-40% of the patients achieve long term remissions. In 2017, in USA, the FDA approved two CD19 different CAR T cells therapies, Axicabtagene ciloleucel (Yescarta) produced by Kite Pharma and Tisagenlecleucel (Kymriah) produced by Novartis, for relapsed and refractory acute lymphoblastic leukemia in children and adults and for diffuse large B-cell lymphoma in adults. One of the main problems of the CAR T cell treatments have been the serious, potentially lethal, side effects associated with this therapy. Currently, CAR T cells are only used in large centers where physicians and the hospital staff completed training for the management of their specific adverse effects (cytokine release syndrome, neurotoxicity, etc). Another challenge in this field has been the treatment of solid tumors with CAR Ts. The results of the studies using Car T cells against several types of solid tumors, i.e. melanoma, cholangiocarcinoma, lung cancer, colorectal cancer, glioblastoma multiforme, etc has been disappointing so far. The main explanations for the lack of efficacy of CAR Ts in solid tumors is their complex environment and their heterogeneity. Currently, CAR T cell treatment of solid tumors is a very active field of research and several techniques of genetic engineering and synthetic biology have been applied both to increase the efficacy of CAR-Ts and to diminish their off-target side effects. The combination of genetic engineering and synthetic biology offers a wide range of possibilities to design “smart” CAR T cells with enhanced functions. Examples: Boolean logic–gated T cells that may recognize either one of two antigens or the two antigens only on the surface of the tumors, CAR-Ts that secrete specific co-stimulatory cytokines, CAR-Ts that have contained controllable suicide switches such as inducible caspase, etc. The efficacy of CAR therapy against B-cell cancers has raised a lot of enthusiasm in the oncology field and currently there are more than 300 studies mainly in China and USA. With more than a thousand patients currently treated in USA, autologous CAR T-cell therapies have demonstrated a promising therapeutic potential, but, at this time, their high costs and the severity of their potential complications limit their use to only few large hospital centers.

14.Alterari genetice si moleculare pentru tratamentul cancerului colorectal metastatic

E. Gabriela Chiorean: University of Washington, Seattle si Fred Hutchinson Cancer Research Center, SUA

Cancerul colorectal este pe locul 2 in ceea ce priveste incidenta si mortalitatea prin cancer in Romania, iar in lume este al 3-lea ca incidenta (1,800,000 anual) si al 2-lea ca mortalitate (880,000 annual). 25% din pacienti sint diagnosticati in stadiu metastatic si 50% din pacientii cu stadiu initial 2-3, operabil, progreseaza cu boala metastatica. Pentru cancerul colorectal metastatic, chimoterapia sta la baza tratamentului si media de viata atinge 3 ani. Anticorpii anti-angiogeni (anti-VEGF and anti-VEGFR) si anti-EGFR (pentru tumori cu KRAS si NRAS wild-type status, unde tumora primara este pe partea stinga a colonului) sint folositi deseori in combinatie cu chimoterapie, si contribuie in medie 3 luni in plus la cresterea supravietuirii. Tratamentele impotriva cancerului in general au evoluat de la terapia nonselectiva cu chimoterapie la terapii tintite, in functie de ce alteratii genetice sau moleculare sint prezente in biopsia solida sau lichida. Putini biomarkeri noi s-au descoperit in ultimii ani pentru cancerul colorectal, cu exceptia RAS, MSI, BRAF si HER2. Recent, tratamentele tintite cu inhibitori de immune checkpoints pentru tumori cu microsateliti instabili (MSI, 3-5% incidenta), cu inhibitori EGFR + BRAF + MEK pentru mutatii BRAF V600E (5-9% incidenta), sau cu terapii anti-HER2 pentru amplificari HER2 (3% incidenta) s-au dovedit eficace. Blocarea de noi tinte, tratamente care sa combata mecanismele de rezistenta la terapiile tintite, si noi modalitati de a sensibiliza cancerul colorectal fara instabilitate microsatelitara la terapii imunologice, sunt arii de cercetare foarte intensa.

15.Avantajele esofagectomiei toracice cu limfadenectomie prin triplu abord total minim invaziv (toracoscopie + laparoscopie)

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Introducere: Esofagectomia reprezintă o procedură chirurgicală majoră cu morbiditate și mortalitate legate de starea pacientului, stadiul bolii, tratamentele complementare și experiența chirurgicală. Esofagectomia minim invazivă poate conduce la scăderea morbiditatii si mortalității perioperatorii cu rezultate precoce foarte bune privind calitatea vieții. **Material și metodă**: Prezentăm experiența Centrului de Excelență în Chirurgia Esofagiană privind esofagectomia minim invazivă prin triplul abord modificat McKeown, integral toraco-laparoscopic, ca experiență inițială, dintr-o serie de proceduri minim invazive pentru neoplasm esofagian. **Rezultate:** În ultimii 3 ani s-au efectuat 17 esofagectomii minim invazive, prin diferite procedee, toracoscopice, asistate laparoscopic și integral toraco-laparoscopice. Prezentăm procedeul minim invaziv integral toraco-laparoscopic de esofagectomie, urmat de reconstrucție esofagiană prin ascensionarea stomacului intratoracic și anastomoză eso-gastrică cervicală și jejunostomie de alimentație. Timpii operatori efectivi au fost: toracic 120 minute, abdominal 130 minute și cervical 50 de minute, cu un total de 300 de minute. Evoluție postoperatorie favorabilă, cu alimentație precoce pe jejunostomie, reluarea tranzitului digestiv după 24 de ore, control al anastomozei cervicale în Z6 și externare Z10 postoperator fără acuze subiective. Controlul la 30 și 90 de zile, fără complicații. **Concluzii:** Experiența solidă în chirurgia esofagiană deschisă asigură o curbă de învățare ce permite realizarea unor proceduri chirurgicale minim invazive complexe, cu morbiditate si mortalitate perioperatorie scazuta. Datorită abordului minim invaziv, evoluția a fost simplă, fără complicațiile specifice unei chirurgii extinse, cu o bună calitate a vieții în postoperator. Urmărirea pe termen lung va putea confirma rezultatele din literatură în ceea ce privește și supraviețuirea, cel puțin echivalentă pentru acești pacienți.

Cuvinte cheie: esofagectomie minim invazivă, triplul abord modificat, toraco-laparoscopic integral

16.Small cell lung cancer- any therapeutic progressis ?

Lucian Miron-UMF „Grigore T. Popa" Iaşi, Institutul Regional de Oncologie Iasi

Small cell lung cancer (SCLC), a smoking-related disease with a poor prognosis is an aggressive tumor characterized by rapid doubling time and high propensity for early development of disseminated disease. Although most patients respond to initial therapy with a platinum doublet, the majority of those with limited stage and virtually all patients with metastatic disease eventually develop tumor progression for which there are limited treatment options. There have been no recent changes in the treatment of SCLC, with platinum plus etoposide and topotecan as the standard first-line and second-line respectively. More recently, a new understanding of the biology of SCLC has led to the development of novel drugs, of which the most promising are the immune checkpoint inhibitors and the antibody drug conjugate rovalpituzumab tesirine. Rovalpituzumab tesirine (Rova-T) is an experimental antibody-drug conjugate targeting the cancer-stem cell-associated delta-like protein 3 (DLL3)1, which is expressed in more than 80% of small-cell lung cancer (SCLC).

Rova-T combines a targeted antibody that delivers a cytotoxic agent directly to the DLL3-expressing cancer cells while minimizing toxicity to healthy cells. Rova-T is under investigation as a third-line treatment in SCLC. The TAHOE trial is a randomized, open-label, two-arm, phase 3 trial assessing the efficacy, safety and tolerability of Rova-T *versus* topotecan in participants with advanced or metastatic small-cell lung cancer (SCLC) with high levels of delta-like protein 3 (DLL3) and who have first disease progression during or following front-line platinum-based chemotherapy. Immunotherapy may provide an opportunity to change the treatment paradigm of SCLC. In 2018, was granted an accelerated approval to single-agent nivolumab (*Opdivo*) for the treatment of patients with SCLC with disease progression following platinum-based chemotherapy and 1 other line of therapy, based on data from the phase I/II CheckMate-032 trial. Pembrolizumab has shown promising antitumor activity and durable responses in advanced SCLC, especially in patients with PD-L1–positive tumors.

The combination of nivolumab and ipilimumab (*Yervoy*) has shown impressive results in SCLC with a high tumor mutational burden (TMB). In an exploratory analysis from CheckMate-032 demonstred an objective response rate (ORR) of 46% in patients with recurrent SCLC with high TMB. This was compared with an ORR of 21% with nivolumab monotherapy. Additionally, data with pembrolizumab (*Keytruda*), atezolizumab (*Tecentriq*), and durvalumab *(Imfinzi*) are expected to read out within the next few years.

PARP inhibitors and ***lurbinectedin*** may have a place in this landscape in the future, either as monotherapy or in combination.

Results of the phase III, **IMpower133 t**rial showed that combining frontline **atezolizumab** with chemotherapy improved overall survival (OS) and progression-free survival (PFS) versus chemotherapy alone in patients with extensive-stage SCLC. The *new* standard of care for the frontline treatment of patients with extensive-stage small cell lung cancer (SCLC) should be atezolizumab (*Tecentriq)* and chemotherapy, based on results from the IMpower133 trial. fThis global, randomized phase III trial demonstrated an improvement in survival with the addition of the PD-L1 inhibitor to standard carboplatin and etoposide in patients with extensive-stage SCLC versus the chemotherapy regimen alone.

17.Revizuire a terapiei cu Inhibitori de Tirozin Kinaza in Cancerul Pulmonar Fara Celule Mici (NSCLC)

CSI Alexandru C. Grigorescu, Institutul Oncologic Bucuresti

In zilele noastre se constata o modificare importanta in terapia sistemica a cancerului pulmonar mai ales a celui fara cellule mici (NSCLC). Terapia tintita cu inhibitori de tirozinkinaza (TKI)pentru pacientii care prezinta mutatii la nivelul genei EGFR a demonstrate ca adduce rezultate mai bune in ceea ce priveste Supravietuirea pana la Progresie (PFS)si Supravietuirea Global(OS). Ulterior au fost sintetizati TKI de generatia a doua si a treia care au dovedit in cateva studii ca duc la rezultate mai bune ale PFS sau OS.

Este in special cazul osimertinibului care este un TKI de generatia a treia, care are si effect asupra mutatiei genei T790 care determina rezistenta la TKI in aproximativ 60% din cazuri.

In acest review am prezentat principalele studii care au consacrat in practica utilizarea TKI si combinatiile cu alte terapii cu scopul de a le creste eficienta si a infrange rezistenta care apare constant la acest tratament.

O alta abordare in acest review a fost prezentarea secventializariii terapiei cu TKI care inca mai suscita la controverse.

Nowadays there is an important change in the systemic therapy of lung cancer, especially of the non-small cell (NSCLC). Tyrosine kinase inhibitors (TKI) therapy for patients with mutations in the EGFR gene has been shown to bring better progression free survival (PFS) and Overal Survival (OS). Later, I presented second and a third generation TKIs that have proven in some studies the best results of PFS or OS. It is particularly the case of osimertinib which is a third-generation TKI, which also has an effect on T790 gene mutation that determines TKI resistance in about 60% of cases. In this review we presented the main studies that have put into practice the use of TKI and combinations with other therapies in order to increase the effectiveness and overcome of the resistance that consistently occurs in this treatment. Another approach in this review was to present the sequencing of TKI therapy that is still controversial.

Key words: Tyrosine kinase inhibitors, Non-Small Cell Lung Cancer, sequential treatment, resistance

18.Actualități in radioterapia stereotaxică în oligometastaze

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Paradigma oligometastatică implică faptul că pacienții care dezvoltă un număr mic de leziuni metastatice pot obține supraviețuirea pe termen lung dacă aceste leziuni sunt tratate prin intervenții chirurgicale sau utilizand radioterapie stereotactică (SBRT). Până de curând, o mare parte din datele justificative pentru o stare oligometastazica au fost retrospective, foarte rar prospective si chiar si mai rar studii randomizate.

În 2018-2019, nu mai puțin de 6 studii randomizate de fază II au fost publicate pentru pacienții cu boală oligometastatică. In marea majoritate in aceste studii s-a utilisat SBRT pentru a trata un număr limitat de metastaze. Pana in prezent, aceste date oferă cele mai puternice dovezi despre starea oligometastatică .

În această prezentare, vom vedea, pe scurt, elementele de bază ale SBRT și studille chirurgicale si radioterapeutice importante retrospective și prospective. In continuare, vom discuta despre studiile randomizate publicate recent. Vom termina cu o discuție despre combinația intre SBRT și imunoterapie.

19.Unique Epigenetic Characteristics of Cancer Stem Cells in Ovarian Cancer

Daniela Matei, MD Northwestern Medine, Feinberg School of Medicine, Chicago, SUA

Development of resistance to chemotherapy was linked to persistence of cancer stem cells (CSCs). CSCs are characterized by the ability to self-renew, grow as spheres, differentiate and generate tumors in immunodeficient mice. They are resistant to traditional forms of treatment, including chemo and radio-therapy. Building on our previous work showing that ovarian CSCs residual after treatment with platinum display increased DNA methylation, we hypothesized that other epigenetic modifications occur, promote a stem-like phenotype, and render CSCs vulnerable to epigenome modifying agents. To begin to address this question, we used partial wave spectroscopy to visualize chromatin at the nanoscale level, the Assay for Transposase Accessible Chromatin with high-throughput sequencing (ATAC-seq) to map accessible promoter regions, and proteomic analysis to measure histone marks in CSCs vs. non-CSCs. We found less open chromatin associated with repressive histone marks in CSCs vs. non-CSC, defined specific gene networks activated in CSCs vs non-CSCs and showed that various epigenetic regulators blocked chromatin compaction and transcription heterogeneity in CSCs. We also identified increased expression of the H379 histone methyl transferase Dot1L in CSCs vs. non-CSCs and demonstrated that Dot1L inhibitors and Dot1L knock down blocked stemness features, including sphere formation, stemness associated transcription factors, and tumorigenicity in vivo. Our data support that epigenetic modifiers suppress CSCs by de-repressing chromatin and promoting activation of differentiation pathways. The results of this project are immediately applicable to ovarian cancer, but may have broader implications for other platinum-resistant solid tumors.

Caracteristicile unice ale celulelor stem in cancerul de ovar

Daniela Matei, MD Northwestern Medine, Feinberg School of Medicine, Chicago, SUA

Rezistenta la chemoterapie a fost conectata cu existenta si persistenta celulelor stem. Celulele stem sunt caracterizate prin capacitatea de a se reinoi permanent, a genera celule diferentiate, a forma sfere si a genera tumori in vivo. Celulele stem sunt rezistente la tratamentul cu chimioterapie sau radiatii. Bazandu-ne pe observatiile noastre preliminare care au demonstrate ca celulele stem sunt caracterizate de o cromatina marcata de metilarea insulelor CpG, am aplicat metodologii noi de secventiere si microscopie celulara pentru a defini cromatina acestei populatii de celule rare. In acest scop am

folosit spectroscopie partiala, analiza proteomica si ATAC-Seq pentru a defini zonele de cromatina deschise si inchise in celulele stem. Pe baza acestor analize, am descoperit ca celulele stem ovariene au o cromatina compacta asociata cu modificari represive ale histonelor. De asemenea, am demonstrat ca celulele stem sunt vulnerabile la tratamentul cu agenti care modifica codul epigenetic, cum ar fi inhibitorii metiltransferazelor. Am aratat ca una dintre metiltransferazele histonelor (Dot1L) functioneaza aberant in celulele stem si ca inhibitorii impotriva acetei enzime au eliminat celulele stem blocand formarea sferelor si a tumorilor in vivo. Rezultatele noastre demonstreaza ca noi agenti care blocheaza codul epigenetic pot de-represa cromatina celulelor canceroase si elimina celulele stem provocand un program de diferentiere celulara. Aceste rezultate sunt aplicabile la cancerul de ovar, dar pot fi aplicate si la alte cancere care devin rezistente la chimioterapie.

20.Metastatic triple negative breast cancers – challenges and opportunities

Dragos Median – Filantropia Clinical Hospital, Bucharest

Triple negative breast cancers, defined by exclusion from others breast cancer subtypes (luminal, Her2-amplified) are considered among the most aggressive malignant neoplasms, mainly due to the lack of targets for current drugs.

The gene analysis identified several actionable mutations or pathways. PARP inhibitors, AKT inhibitors, immune checkpoints inhibitors or antibody-drug conjugates are some promising agents approved in clinical practice or in different phases of development, making the future in the treatment of this condition more optimistic.

21.Iradierea accelerată, parțială a sânului

Gabriel Ricu, MD Amethyst Radiotherapy Centre

Radioterapia joacă un rol important în tratamentul cancerului mamar. In special după chirurgia conservatoare, iradierea întregului san, ocazional cu suplimentarea dozei la nivelul patului tumoral, face parte integrantă din terapia conservatoarea a sânului. La sfârșitul anilor 1990, o nouă abordare a fracționării isi face loc în tratamentul postoperator: hipofracționarea cu o doză totală redusă la 39-42,6 Gy în 13-16 fracții administrate în decurs de 3 săptămâni. Aceasta fractionare este acum larg acceptată ca o metodă standard pentru WBI. În plus, încercând să scadem si mai mult timpul de tratament și volumul iradiat, păstrând ratele de control local ale iradierii totale a sanului (WBI), apare si evolueaza rapid o noua si atractiva abordare - iradierea parțială accelerată a sanului (APBI). Rationamentul care sta la baza APBI este acela de a intensifica tratamentul în zona cea mai expusă riscului de recurență, tratând doar partea afectata a sânului cu scopul de a controla cancerul, a reduce efectele secundare și a îmbunătăți calitatea vieții.

Iradierea parțială accelerată a sanului(APBI) este evaluata in studii clinice de aproape 20 de ani. Există mai multe tehnici de administrare a iradierii ce si-au dovedit eficacitatea in practica: brahiterapie, radioterapie intraoperatorie (IORT) sau iradiere externa (3D-CRT sau IMRT). Datele nu sunt insa suficiente pentru a favoriza în mod clar una dintre aceste tehnici, fiind necesare studii suplimentare pentru a determina tehnica optimă în ceea ce privește controlul local pe termen lung, efectele secundare și pentru a defini cea mai bună abordare pentru fiecare pacient in parte.

Înțelegerea radiobiologiei, tehnicile de iradiere, criteriile de selecție a pacientelor și metodele de evaluare imagistica au progresat ori s-au imbunatatit semnificativ pe parcursul desfasurarii studiilor clinice. Dupa finalizarea studiilor de fază III cu urmărire pe termen lung, APBI este utilizata din ce în ce mai frecvent fie în studiile de fază IV, fie la pacienții selectați în practica clinică de rutină în afara studiilor clinice.

În prezent avem ghiduri privind criteriile adecvate de selecție a pacienților, elaborate de societățile naționale și internaționale precum ESTRO, ASTRO și DEGRO, acestea insa trebuie să fie armonizate între țări și intre diferitele tehnici de administrare a iradierii. Criteriile corecte de selecție ale pacientelor pentru APBI și armonizarea fractionarilor folosite vor simplifica semnificativ compararea datelor din diferite studii.

22.Whole Body MRI - Its role in the detection and post-therapeutic tracking of bone metastases in the high-precision oncology era

Virgil Ionescu - Monza-Metropolitan Hospital Bucharest-Romania

The goal of this presentation is to propose to oncology clinicians a new paradigm in the imagistic approach of a newly discovered breast cancer patient as well as in the follow-up of cases already known during therapy and post-therapy.

General drivers for WB-MRI in oncology practice are:

(1) poor performance of conventional imaging when detecting disease, assessing tumour volume or therapy response and

(2) poor performance of serum markers in assessing response - CA 15-3 in breast cancer, PSA in castrate resistant prostate cancer, etc

Current imaging tools lead to poor confidence for assigning clinical states and addressing therapy benefits.

They are limited tools because:

- are unable to accurately depict metastatic disease presence or extent;

- have limited ability to depict heterogeneity of response in patients with bone disease;

- are unable to identify who is not benefiting early after starting treatment.

MET-RADS - standard for WB-MRI in metastatic cancer will develop new criteria to asses metastatic bone disease. WB-MRI have the potential to alter diagnostic thinking when assessing response by adding categories that positively assess the success of therapies in bone disease (NOT just absence of progression).WB-MRI could help deliver the promise of precision oncology for patients with malignant bone disease - “right treatment, right patient, right time 4 the right duration”. Validation and qualifications are currently incomplete.

23.Tratamentul cancerului de col uterin

Alina Sturdza, MD, FRCPC, AKH Viena, Medicinische Universität Wien, Austria

In Europa 61/100000 femei sunt diagnosticate anual cu cancer de col uterin si o treime mor din cauza acestei boli. Desi in multe tari exista screening sistematic, incidenta sa variaza larg intre 4.4- (Malta) si 28.7/100000 (Bosnia Herzegovina)[1].

In Romania cancerul de col uterin ocupa locul trei ca incidenta dupa cel de sin si colorectal cu 26/100000 cazuri din care jumatate mor anual. Din pacate, in lipsa screeningului anual, majoritatea cancerelor de col uterin sunt diagnosticate in stadii avansate cind tumorile sunt deja mari si incep sa produca simptome.

Din fericire insa, medicina moderna detine tratamente foarte eficiente pentru aceasta boala. Tratamentul este multidisciplinar, implicind ginecologul oncolog, chimioterapeutul si radio-oncologul. In Europa exista din 2018 guidelines care au fost concepute in acest cadru multidisciplinar[2]. De asemenea la sfirsitul anului trecut s-a actualizat stadiul FIGO care in mod istoric se baza pe stadializarea tumorii numai prin examenul clinic. In noul stadiu se accepta si folosirea imagisticii (de ex. RMN, PET-CT etc)[3]. Pe scurt, cancerele microscopice si macroscopice cu dimensiuni mici, sub 4 cm se trateaza chirurgical, iar cele local avansate sau cu dimensiuni mici, dar cu noduli limfatici pozitivi diagnosticati fie prin examen pathologic sau imagistic, se trateaza cu radiochemotherapie. Aceasta consta din radiatii externe ale unui volum care contine tumora, uterul, parametriile si o parte din vagin, plus nodulii limfatici pelvini ± para-aortali pina la o doza microscopica de 45 de Gy. Daca nodulii limfatici sunt suspecti, se recomanda un boost integrat sau secvential, pina la o doza de 60 Gy in zona nodulului limfatic respectiv. In paralel se aplica chimioterapie cu Cisplatin 40 mg m^2/SC saptaminal, pentru minimul 5 cicluri. Apoi se aplica un boost in regiunea tumorii si a ariilor care inca mai pot contine tumora microscopica pina la o doza de minimum 85Gy prin brachiterapie. Durata tratamentului trebuie sa fie maxim 50 de zile calendaristice

(ideal 45 zile), altfel se pierde din eficacitatea preconizata[4]. “State of the art” este ca terapia externa sa fie facuta printr-o tehnica moderna care protejeaza organele la risc, IMRT, VMAT, IMAT si brachiterapia cu ghidaj RMN, sau unde nu este accesibil, cu CT. Rezultatele cu ghidaj imagistic, in special al brachiterapiei, sunt excelente, cu control local al tumorii de peste 90% la 5 ani (in tumorile mici de 98%, iar in stadiile foarte avansate de 75%)[5]. Speram ca aceste tehnici o sa fie accesibile in cit mai multe centre din Romania si ca impreuna cu crearea unui program de screening si de vaccinare anti-HPV incidenta si mortalitatea datorita cancerului de col uterin sa scada vertiginos.

[1] Ferlay J, Colombet M, Soerjomataram I, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. European journal of cancer (Oxford, England : 1990). 2018;103:356-87.
[2] Cibula D, Potter R, Planchamp F, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology Guidelines for the Management of Patients With Cervical Cancer. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2018;28(4):641-55.
[3] Bhatla N, Aoki D, Sharma DN, et al. Cancer of the cervix uteri. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2018;143 Suppl 2:22-36.
[4] Tanderup K, Fokdal LU, Sturdza A, et al. Effect of tumor dose, volume and overall treatment time on local control after radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology. 2016;120(3):441-6.
[5] Sturdza A, Potter R, Fokdal LU, et al. Image guided brachytherapy in locally advanced cervical cancer: Improved pelvic control and survival in RetroEMBRACE, a multicenter cohort study. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology. 2016;120(3):428-33.

24.Răspunsuri terapeutice particulare la imunoterapie - prezentări cazuri clinice

Michael Schenker ,UMF Craiova, Disciplina Oncologie

Ultimii ani au însemnat o adevărată revoluție a standardelor de tratament în cele mai importante (frecvente) cancer solide. Acest fenomen s-a datorat atât unor noi medicamente încadrate în categoria terapiei țintite molecular dar și, mai ales, imunoterapiei. Inhibitorii antiPD1 și antiPDL1, prin multitudinea de noi indicații terapeutice achiziționate, dar și prin rapiditatea cu care s-au impus ca noi standarde pentru indicațiile respective, sunt, foarte probabil, un moment unic în dezvoltarea din ultimii 20 de ani a oncologiei. Până în prezent, nici un alt medicament nu a beneficiat de atâtea înregistrări noi din partea agențiilor guvernamentale, în termen atât de scurt, precum pembrolizumab si nivolumab. O varietate de studii clinice de fază IIB, III sau IV au fost disponibile în ultimii ani și sunt, în continuare, o importantă soluție de tratament pentru mulți dintre pacienții noștri. Tipul de studiu clinic de faza IV, care urmărește evaluarea siguranței unui medicament recent înregistrat, la un număr mare de pacienți, a reprezentat și reprezintă încă, o opțiune terapeutică foarte atractivă pentru pacienții noștri, având în vedere că suntem încă mult în urmă, ca țară, în ceea ce privește susținerea financiară a acestor noi indicații pentru acești modulatori ai răspunsului imunitar anti-tumoral (de ex: cancere ale sferei ORL, cancer pulmonar - linia 1 asociat sau nu chimioterapiei sau unui alt modulator al răspunsului imunitar, gen blocant al receptorilor CTLA4, carcinoame uroteliale, cancer gastric, carcinoame renale cu celule clare - linia 1 asociate cu o moleculă țintită gen axitinib sau cabozantinib și multe alte indicații). În cadrul Centrului de Oncologie Sf Nectarie Craiova, între anii 2014 și 2019, un număr de peste 400 de pacienți au beneficiat de o metodă de tratament care a conținut cel puțin un modulator al răspunsului imunitar anti-tumoral. Cei mai mulți dintre acești pacienți au fost tratați în trialuri clinice, numai 10-15% beneficiind de aceste terapii prin Program Național.

Orice metoda nouă de tratament aduce cu sine numeroase situații particulare, atât în ceea ce privește tipul de răspuns, efectele secundare sau influențarea calității vieții. Aceste situații particulare sunt mai evidente in cazul acestei noi metode de tratament a cancerului comparativ cu tratamentul chimioterapic sau cu cel țintit molecular.

Prezentarea din cadrul conferinței “Stop Cancer 2019”, își dorește să ilustreze aceste particularități, prin exemple concrete, cazuri clinice, pacienți tratați în cadrul Centrului de Oncologie Sf Nectarie Craiova, în perioada 2014-2019. Vor fi prezentate cazuri care descriu fenomenul de “falsă progresie”, pacienți care au prezentat răspuns favorabil la câteva luni după progresia radiologică, efecte secundare particulare (ex - hipofizită) și managementul acestora, pacienți cu răspuns terapeutic favorabil foarte rapid si intens, etc.

25.Transformarea neuroendocrina in tumori – transdiferentiere sau heterogenitate tumorala?

Carmen Ardeleanu[1, 2], Florin Bacanu[3], Dana Terzea[1]

1.Onco Team Diagnostic, UMF "Carol Davila" Bucuresti 2.Royal Hospital Bucuresti,

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Caracterul neuroendocrin al tumorilor provenite din diferite organe imprima anumite particularitati care influenteaza atat modul lor de producere cat si denumirea lor. Astfel, tumorile din organe cu celule cu secretie neuroendocrina (medulosuprarenala, paratiroidele, tiroida sau chiar tubul digestiv si pulmonul), au celule de origine specifice si sunt clasificate in functie de anumiti parametri, in tumori neuroendocrine bine, moderat sau slab diferentiate. Pentru organele in care nu se evidentiaza curent celule neuroendocrine (glanda mamara, prostata, rinichiul, colul uterin) celula de origine este dificil de stabilit in cazul aparitiei unei tumori cu imunofenotip neuroendocrin. De aceea clasificarile acestora cuprind tumori neuroendocrine si tumori cu caracter/diferentiere neuroendocrina (Rosen, 2017). Exista insa posibilitatea aparitiei unei tumori neuroendocrine in recidiva unei tumori epiteliale de exemplu la prostata, glanda mamara sau plaman. Se poate considera ca aparitia lor se realizeaza printr-un proces de transdiferentiere, sub influenta unor factori transcriptionali ai unor gene de celule stem, ca de ex. SOX2 (Karachaliou, 2013). Totusi nu se poate exclude posibilitatea ca in orice tumora epiteliala sa existe initial (conform heterogenitatii tumorale) un numar de celule cu caracter neuroendocrin care in cursul expansiunii clonale tumorale sa se activeze (Kato, 2019). Procesul de transdiferentiere a fost studiat experimental fiind identificati o serie de factori transcriptionali care intervin in caile de semnalizare legate de diferentiere si proliferare ca de ex. Wtn/beta-Catenina (Sinner, 2004), EGFR-Src-AKT (Singh, 2012), IL8-CXCRC2-p53 (Huang, 2005), PI3K-AKT-mTOR (Lee, 2016), IL6-STAT3 (Yao, 2018), MAPK-ERK etc. Un model cunoscut de transformare neuroendocrina este cel din carcinomul de prostata, secundar terapiilor antiandrogenice. Toti acesti factori care produc transformarea ar putea sa devina tinte terapeutice.

26.Hematopoietic versus nonhematopoietic tumors: That is the question

Gabriela Gheorghe: Children's Hospital Minnesota, SUA

The traditional morphology-based classification of hematologic neoplasms is currently complemented by an ever-increasing array of immunophenotypic, cytogenetic and molecular markers. The current WHO classification establishes the guidelines for an integrated diagnosis combining clinical data, morphology, immunophenotyping and genetic features of hematological malignancies. Adequate clinical management relies on both diagnostic accuracy and an expanding number of targeted therapeutic agents geared towards underlying pathological and molecular abnormalities responsible for tumorigenesis. In contrast, the risk of diagnostic errors in hematology persists due to both technical errors and lack of expertise. This presentation reviews a range of potential pitfalls in the diagnosis of hematological malignancies. For example, nonspecific staining of blasts with nonhematopoietic antigens such as vimentin, HMB-45, thyroglobulin, and actin should not be misinterpreted as evidence of metastatic carcinoma. Neuroendocrine tumors are typically positive for CD56, but like all epithelial neoplasms, they are consistently CD45 negative and positive for other epithelial markers. Awareness of such pitfalls, some common while others are rare carries vital clinical importance in disease management. Arriving to a final diagnosis of a hematological malignancy relies upon a combination of clinical information, good laboratory techniques, access to appropriate diagnostic tools, good communication with our clinical colleagues and the experience of the hematopathologist.

27.Tratamentul durerii la pacientul oncologic

Dr. Ovidiu Palea-Provita

Tratamentul durerii la pacientul oncologic este o prioritate pentru echipa medicala. Atat din punct de vedere al calitatii vietii cat si al raspunsului imun si al luptei organismului contra bolii, controlul durerii are un impact major asupra rezultatului terapeutic. Interventiile minim invazive sunt intr o expansiune majora si vin in ajutorul pacientului cu solutii reale si pe termen lung, cu efecte secundare minime si complicatii asumabile in fata alternativelor medicale sau chirurgicale.

Romania se aliniaza astazi si in acest domeniu tarilor avansate.

28.Stem Cell Therapies for the Treatment of Cancer

Daniela A. Bota University of California, Irvine, SUA

Malignant disorders are characterized by a complex hierarchy, with tumorigenic cancer stem cells (CSCs) controlling tumor proliferation and treatment resistance. The CSCs can differentiate into non-tumorigenic progenies and in transdifferentiated, neoplastic blood vessels. The modern oncological treatments have the goal of eradicating the CSCs, using complex approaches, such as targeted molecules which address the specific stem cell pathways, monoclonal antibodies targeted to the stem cell markers present on the CSCs surface, and CAR-T cells with the ability to reduce the CSCs burden.

Normal stem cell biology can also be explored for the treatment of multiple malignancies. From using neural stem cells to deliver therapies to malignant gliomas to harvesting hematopoietic stem cells to produce a genetically modified immune system that can target and eliminate blood malignancies, novel treatments are currently developed. The recent approval of the CART therapies Yescarta (axicabtagene ciloleucel) and Kymriah (tisagenlecleucel) has led to durable responses and possible cures for acute lymphoblastic leukemia.

In this new era of hope, questions still linger about the costs of the therapies we currently develop which many times are measured in hundreds of thousands of dollars for each patient. How the access to these therapies will be extended to all patients in need remains an important topic for establishing public policies across multiple countries.

29. Immunotherapies and vaccines for the treatment of Brain Malignancies

Daniela A. Bota University of California, Irvine, SUA

New discoveries in the field of cancer biology have greatly expanded the therapeutic options available for patients with primary and metastatic brain tumors. With novel, targeted options becoming available at an accelerated pace, the role of each modality such as radiation, classical chemotherapy, targeted agents and immunotherapy in the treatment plan must be reviewed considering current evidence.

The last years have revolutionized the field on cancer immunotherapies, with novel treatments being approved almost every month for a variety of malignancies, including melanoma, lung cancer, bladder cancer, etc. However, despite multiple phase III studies, no GBM immunotherapy has been able to show effectiveness and to obtain FDA approval. Many approaches have been used, including vaccines targeting different antigens on the cell surface, or whole cell antigens repertoires.

Our approach brings a different concept – namely the use of a broad-antigen-based approach, including both allogeneic and autologous components and shows promise in activating a very important population of cells – namely the the CD4+ helper T lymphocytes. The future promise of our treatment might also rest in the ability to combine it with bevacizumab, and potentially with immune checkpoint inhibitors – an option that will allow more powerful immune activation in the periphery as well as more aggressive local tumor immunological targeting and destruction

Discussing the role of immunotherapy in an immuno-privileged area such as the brain remains an active topic of research.

Notes

Al 4-lea Simpozion de Oncologie Translaţională Personalizată pentru combaterea cancerului

SIMPOZION VIRTUAL

2020

Organizat:

Asociația STOP Cancer

DIRECTORI SIMPOZION:

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