

13th INTERNATIONAL
CONGRESS
OF THE SERBIAN SOCIETY
OF TOXICOLOGY



1st TOXSEE
REGIONAL
CONFERENCE

Present and Future of toxicology: Challenges and opportunities



10 - 12 May, 2023 Belgrade

electronic

ABSTRACT
BOOK

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13th INTERNATIONAL
CONGRESS
OF THE SERBIAN SOCIETY
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&

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Conference

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DEAR COLLEAGUES, DEAR FRIENDS,

We are delighted to greet you on the **13th International Congress of the Serbian Society of Toxicology & 1. TOXSEE Regional Conference - Present and Future of toxicology: challenges and opportunities**, organized in Belgrade from 10-12 May 2023.

Five years after our last international Congress we gathered in Belgrade, to further promote contemporary toxicology, in the broadest sense of meaning, as a response to the new challenges requiring innovative approaches and solutions, as it is understood in the third decade of the XXI century.

Initial concept, to blend the top scientific level in toxicology with the potentials of its' use in broad array of clinical and other domains, proved to be right. Line-up of more than 70 first class international and regional faculties as well as best Serbian scientists and toxicology professionals in all related domains fully justify the approach. Moreover, interest and presence of more than 250 colleagues from Serbia and region witness that our professional community has recognized the approach taken and shown vast interest.

The Serbian Society of Toxicology is committed to innovation and creativity in research and education, in cooperation with collegial associations and institutions in Serbia and abroad. As a regional leader, we developed and inaugurated the regional brand TOXSEE, with the idea to gather as much as possible expertise and know-how from the region and Europe, to capture knowledge, share experience and exchange practical skills with colleagues who deal with toxicology problems daily.

Time imposes on us the need to integrate science, top knowledge and daily practice in a quality and efficient way, to contribute to the better health of the society as a whole in the most purposeful manner. Therefore, a thematic and functional connections with domains of emergency medicine, general medicine, paediatrics, ecology, in addition to already standard toxicological disciplines i.e. clinical, forensic, occupational, and experimental toxicology have been enhanced.

We are glad to host you in a pleasant atmosphere of Belgrade in mid-May, to benefit from the attractive and dynamic program, exchange knowledge, and, equally important, to refresh existing and establish new contacts with colleagues and friends, while enjoying our hospitality and cherish the moment in one of the best partying cities of Europe.

YOU ARE MOST WELCOME!!!



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- President of the STC
- President of the 13th STC Congress

Petar Bulat



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- President of the COC
of the 13th STC Congress

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POSTOJI LI VEZA IZMEĐU HEMATOLOŠKE TOKSIČNOSTI I ODGOVORA NA NEOADJUVANTNU HEMORADIOTERAPIJU KOD PACIJENATA SA LOKALNO UZNAPREDOVALIM KARCINOMOM REKTUMA?

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Standardni tretman lokalno uznapredovalog karcinoma rektuma (LARC) je neoadjuvantna hemioradioterapija (nCRT), nakon čega sledi operacija. Cilj ove studije bio je da se proceni povezanost između hematološke toksičnosti i odgovora tumora na terapiju (TR). U periodu od juna 2020. do januara 2022. godine, u studije je prospektivno uključeno 75 pacijenata sa LARC-om koji su lečeni dugotrajnim režimom CRT-a. RT je isporučena korišćenjem volumnog rotacionog planiranja zračne terapije i simultanog integrisanog boost-a. Istovremena hemioterapija (5-FU, leukovorin) je primenjivana tokom prve i pete nedelje RT. TR je procenjen u 8. nedelji, nakon završetka nCRT. Za pacijente sa potpunim kliničkim odgovorom (cCR) nije predložena neposredna radikalna operacija.



Grupa pacijenata koja je dobro odgovorila na sprovedeno lečenje (eng. responders, R) je definisana sa cCR i TRG1 i TRG2 postoperativnim kategorijama, prema Mandardovoj klasifikaciji. Grupa koja je lošije odgovorila (eng. non-responders, NR) definisana je kao TRG3-5. Akutna toksičnost je procenjivana nedeljno u skladu sa zajedničkim terminološkim kriterijumima za neželjene događaje (CTCAE) v.5.0. R su obuhvatali 46,6% pacijenata.

Tokom nCRT, javili su se ukupni hematološki neželjeni efekti: anemija 40,0%, leukopenija 32,0% i neutropenija 21,3%. Anemija 3. stepena, leukopenija i neutropenija su se javile kod 6,7%, 2,7% i 4% pacijenata, respektivno. Nije prijavljena toksičnost 4. stepena. Limfopenija je primećena kod 94,7% pacijenata; 50,7% njih imalo je stepen toksičnosti 3/4. Značajna povezanost između hematološke toksičnosti i TR nije dokazana. Negativan trend je primećen kod anemije; pacijenti bez anemije tokom nCRT bolje su reagovali na lečenje ($p=0,05$). Ova povezanost može biti dovedena u vezu sa hipoksijom tumora i posledičnom radiorezistentnošću. Limfopenija izazvana zračenjem i njena potencijalna povezanost sa TR biće ispitana u nastavku ove studije. Dalje analize će biti usmerene na ispitivanje subpopulacija zahvaćenih limfocita korišćenjem CyTOF metodologije masene citometrije.

KLJUČNE REČI: lokalno uznapredovali karcinom rektuma, neoadjuvantna hemioradioterapija, hematološka toksičnost.

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IS THERE A RELATION BETWEEN HEMATOLOGICAL TOXICITY AND RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER?

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The standard treatment for locally advanced rectal cancer (LARC) is neoadjuvant chemoradiotherapy (nCRT) followed by surgery. The aim of this study was to evaluate the association between different hematological toxicity and tumor response (TR). We prospectively included 75 LARC patients treated with long-course CRT between June 2020 and January 2022. RT was delivered using volumetric modulated arc therapy-simultaneous integrated boost. Concomitant chemotherapy (5FU, Leucovorine) was given during the first and fifth week of RT. TR was assessed in week 8, after nCRT completion. No immediate radical surgery was suggested for patients with complete clinical response (cCR). Responders were defined as patients with cCR and TRG1 and TRG2 postoperative categories, according to the classification by Mandart. Non-responders were classified as TRG3-5. Acute toxicity was evaluated weekly according to common terminology criteria for adverse events (CTCAE) v.5.0.



Responders group comprised 46.6% of patients. During nCRT, all-grade hematological adverse effects occurred: anemia 40.0%, leukopenia 32% and neutropenia 21.3%. Grade 3 anemia, leukopenia and neutropenia occurred in 6.7%, 2.7% and 4% of patients, respectively. No grade 4 toxicity was reported. Lymphopenia was observed in 94.7% of patients; 50.7% of them had grade 3/4 toxicity. No significant association was found between hematological toxicities and TR.

A negative trend was observed for anemia; patients without anemia during nCRT responded better to treatment ($p=0.05$). This association might be connected to tumor hypoxia and consequent radioresistance. Radiation-induced lymphopenia and its potential association with TR remain to be understood. Further analyses will be directed to the investigation of the affected lymphocytes subpopulations using a CyTOF mass cytometry methodology.

KEY WORDS: locally advanced rectal cancer, neoadjuvant chemoradiotherapy, hematological toxicities.

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