

BEST OF HDIO 2024

Nagrade za najbolje radove

3. NAGRADA I

Avelumab kao terapija održavanja u uznapredovalom urotelnom karcinomu – ažurirana hrvatska iskustva

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Avelumab as maintenance after platinum-based chemotherapy in patients with advanced urothelial cancer (aUC) – updated results from Croatian Uro-Oncology Collaborative Group (CUOOCG) on 115 patients

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INTRODUCTION

Platinum-based chemotherapy followed by avelumab switch maintenance in non-progressors is the standard of care first line treatment for advanced urothelial cancer (aUC). Aim of this study was to assess clinical characteristics and outcomes in a 'real-world' cohort of patients treated with avelumab maintenance for aUC within Croatian Uro-Oncology Collaborative Group (CUOOCG).

PATIENTS AND METHODS

- Retrospective cohort study included patients treated with maintenance avelumab after platinum-based chemotherapy for aUC at 10 CUOOCG-affiliated institutions
- Updated progression-free survival (PFS), overall survival (OS) and toxicity were presented
- Clinical variables of special interest were analyzed
- Median follow-up 13 months

Table 1. Basic patient characteristics

Variable	N = 115
Age, median (range)	70 (43 – 84)
Sex, n (%)	
Male	85 (74)
Female	30 (26)
Location of primary tumor, n (%)	
Bladder	95 (83)
Upper tract	20 (17)
Tumor histology, n (%)	
Pure urothelial carcinoma	85 (75)
Urothelial carcinoma with variant	30 (25)
Presence of metastasis at diagnosis, n (%)	
Yes	55 (48)
No	60 (52)
Metastasis site, n (%)	
Lymph node	70 (61)
Liver	19 (17)
Lung	48 (42)
Bone	29 (25)
Other	15 (13)
ECOG PS at start of 1L chemotherapy, n (%)	
0	73 (63)
1	40 (35)
2	2 (1)
Type of 1L chemotherapy, n (%)	
Cisplatin + gemcitabine	70 (61)
Carboplatin + gemcitabine	30 (26)
ddMVAC	12 (10)
cisplatin > carboplatin + gemcitabine	3 (3)
No. of 1L chemotherapy cycles, median (range)	4 (3-12)
Response to 1L chemotherapy, n (%)	
Complete response	6 (5)
Partial response	65 (57)
Stable disease	41 (36)
Unknown	3 (2)
Time from end of chemotherapy to initiation of avelumab, n (%)	
< 4 weeks	18 (16)
> 4 weeks	97 (84)
ECOG PS at start avelumab, n (%)	
0	74 (64)
1	40 (34)
2	1 (1)

RESULTS

Figure 1. Avelumab th duration (median 6 mo)



Figure 2. PFS curve (median PFS 12 mo)

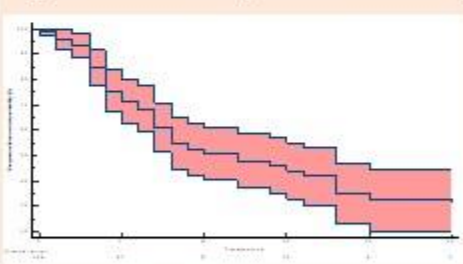


Figure 3. OS curve (median NR)

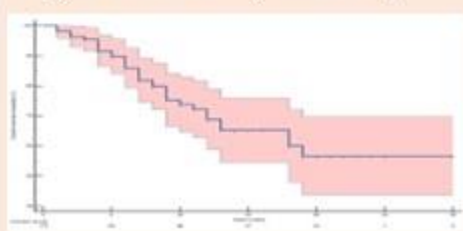


Figure 4. No of chemo cy and PFS

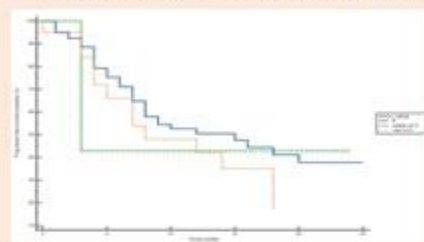


Figure 5. Type of chemo and PFS

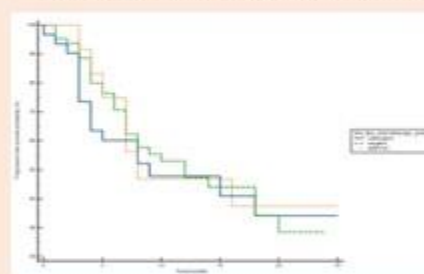


Figure 6. Response to chemo and PFS

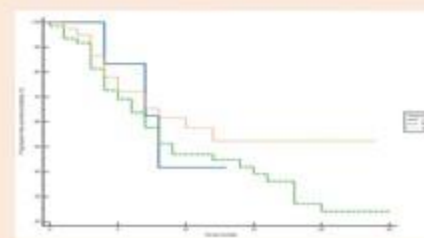
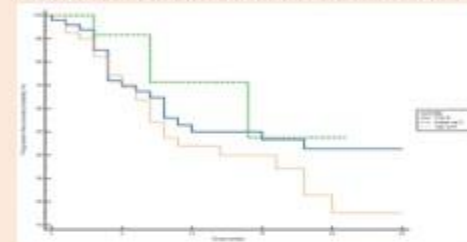


Figure 7. End of chemo-ave start and PFS



- ORR with avelumab maintenance was 20% (CR 4%, PR 16%, SD 38%).
- 55 patients (47%) experienced disease progression.
- 54 patients still on avelumab treatment
- Incidence of immunotherapy-related side-effects was 21% for grade 2, 6% for grade 3, and 2% for grade 4
- 8 patients permanently discontinued Ave due to SAE
- 16 patients received active therapy post ave progression

CONCLUSIONS

- High prevalence of cisplatin-based chemotherapy in our population
- All patients subgroups benefit
- Lower toxicity compared to registration trial

3. NAGRADA II

“Sentinel Uma” – projekt za zaštitu mentalnog zdravlja liječnika i drugih zdravstvenih djelatnika

Petra Sertić, Lea Murn, Karla Zekulić, Lana Skorić, Mario Nalbani



Sentinel Uma

“Sentinel Uma” - projekt za zaštitu mentalnog zdravlja liječnika i drugih zdravstvenih djelatnika

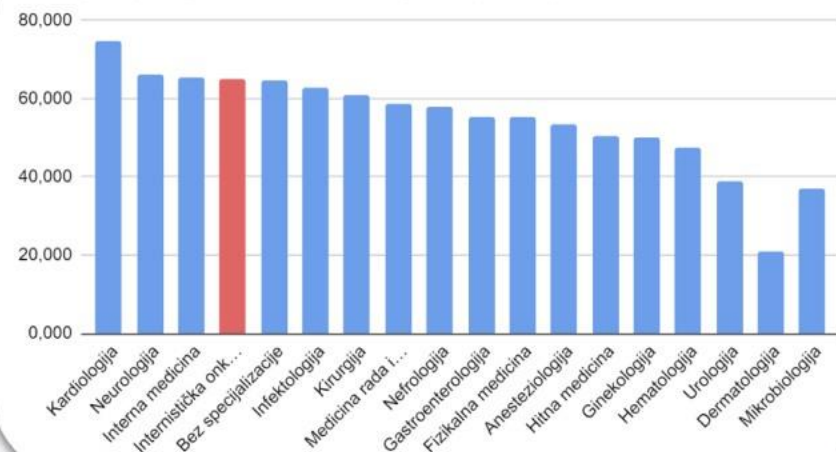
Petra Sertić 1, Lea Murn 2, Karla Zekulić 1, Lana Skorić 2, Mario Nalbani 3

1 Zavod za internističku onkologiju, Klinika za tumore, KBC Sestre milosrdnice, Zagreb, 2 Zavod za psihijatriju, Klinička bolnica Dubrava, 3 Odjel za onkologiju, Opća bolnica Dubrovnik

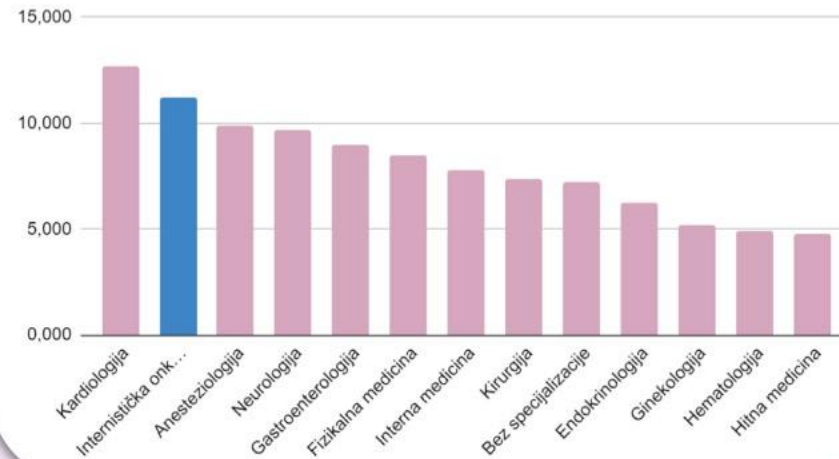


Uvod: Projekt "Sentinel Uma," pokrenut je od strane Sekcije mladih onkologa HDIO uz podršku Sekcije mladih psihijataru HPD-a s ciljem destigmatizacije i zaštite mentalnog zdravlja liječnika i svih zdravstvenih djelatnika. Zdravstveni su djelatnici izloženi visokim razinama stresa što često dovodi do sindroma sagorijevanja. Djelatnici koji zbrinjavaju onkološke bolesnike redovito su izloženi traumatičnim situacijama, bilo da se radi o teško bolesnim pacijentima, smrti ili emocionalno zahtjevnom komunikacijom o lošim vijestima. Administrativna opterećenja, manjak resursa i sustavna ograničenja mogu dovesti do bespomoćnosti, moralnog distresa i moralne ozljede. Moralni distres nastaje kada zdravstveni djelatnici znaju što je ispravno, ali su spriječeni djelovati u skladu s moralnim uvjerenjima zbog vanjskih ograničenja, a moralna ozljeda odnosi se na psihološke posljedice koje proizlaze iz osjećaja krivnje zbog izdaje etičkih uvjerenja ili postupaka koje su poduzeli.

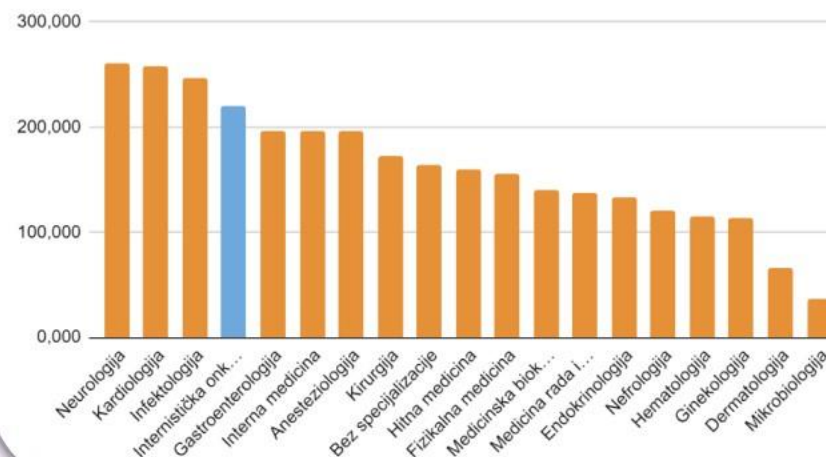
Rangiranje Mjera Moralne Ozljede (MISS)



Rangiranje specijalizacija prema A_DASS (Anksioznost):



Rangiranje Mjera Moralnog Distresa (MMD)



Metode i rezultati: U sklopu projekta "Sentinel Uma" provodi se istraživanje o moralnom distresu i moralnoj ozljedi, te njihovoj povezanosti sa stresom, anksioznošću i depresijom. U istraživanju je dosad sudjelovalo 169 zdravstvenih djelatnika, koji su prijavili umjerene razine anksioznosti, depresije i moralne ozljede, te visoke razine stresa i moralnog distresa. Liječnici u neurologiji, kardiologiji, infektologiji i internističkoj onkologiji izloženi su najvišim razinama moralnog distresa i moralne ozljede prvenstveno zbog suočavanja s terminalnim pacijentima, donošenja odluka o prekidu terapije i ograničenja u resursima.

Zaključak: Ovi pilot rezultati ukazuju na potrebu za sustavnim intervencijama koje uključuju psihološku podršku zdravstvenih djelatnika, osobito u visokorizičnim specijalizacijama kao što je internistička onkologija, uz pružanje etičkih savjeta i obuke za suočavanje s izazovima. Uzimajući u obzir dobivene rezultate, u daljnjim koracima ovog projekta, ciljevi će biti podići svijest o važnosti kontinuirane skrbi o mentalnom zdravlju kroz psioedukaciju zdravstvenih djelatnika i šire javnosti o izazovima mentalnog zdravlja te predložiti konkretne korake za pomoć u izazovima s kojima se zdravstveni djelatnici svakodnevno suočavaju.

2. NAGRADA

Sveobuhvatno gensko profiliranje u bolesnika s uznapredovalim urotelnim karcinomom: prvi rezultati hrvatske uro-onkološke mreže

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COMPREHENSIVE GENOMIC PROFILING (CGP) IN PATIENTS WITH ADVANCED UROTHELIAL CANCER (aUC): FIRST RESULTS FROM CROATIAN URO-ONCOLOGY NETWORK (N=74)

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INTRODUCTION

- The aim of this study was to assess uptake and implementation of CGP in everyday clinical practice of patients with aUC

PATIENTS AND METHODS

- Data from six centres were retrospectively analyzed for utilization of CGP during the standard-of-care treatment of patients with aUC
- The primary endpoint was feasibility of CGP in real-world setting using FoundationOne platform
- The secondary endpoint was to assess the mutation profile of our patients with aUC and to identify patients who may benefit from targeted therapy

RESULTS

Figure 1. Gene mutation map (N=66 samples)

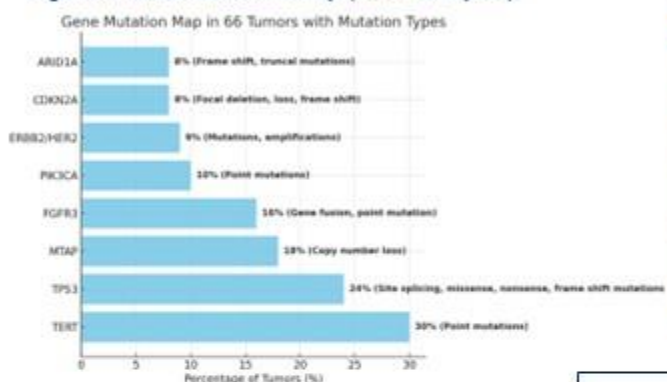


Table 3. Efficacy of targeted therapy (N=7)

Pathogenic alteration	Targeted therapy	line	Best response	PFS (months)	OS (months)	Vital status
FGFR3 - S249C	Pemigatinib	IV	SD	7	9	Deceased
ERBB2	Trastuzumab deruxtecan	III	SD	8	8	Alive on treatment
FGFR3 Y373C	Pemigatinib	II	PR	6	9	Deceased
FGFR3 - S249C	Pemigatinib	III	PD	1	1	Deceased
BRCA1	Olaparib	II	PD	2	6	Deceased
FGFR3 - S249C	Pemigatinib	IV	SD	7	9	Deceased
ERBB2	Trastuzumab deruxtecan	IV	PR	8	9	Deceased

Figure 4. PFS on ICI and TMB

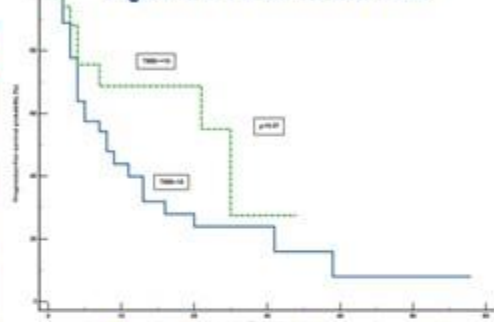
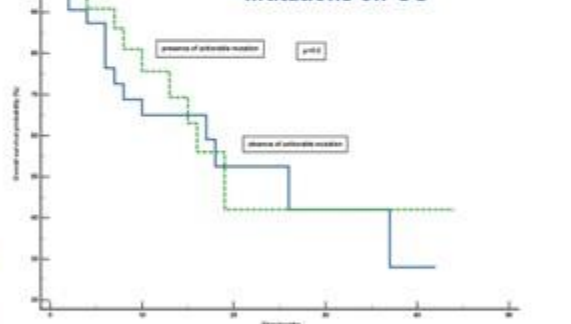


Figure 5. Impact of presence of actionable mutations on OS



- ✓ Patients with TMB > 10 mut/Mb (N=24) had numerically higher response rates and overall survival on immunotherapy
- ✓ TMB median range was 7 (0-65)
- ✓ MSI high N=1 (1%)

Figure 2. Comparison of most common mutations: 66 Tumors vs TCGA Bladder Cancer

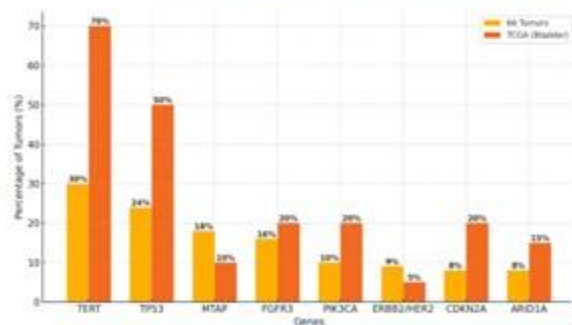


Figure 3. Response rate on ICI (TMB ≥ 10 vs TMB < 10)

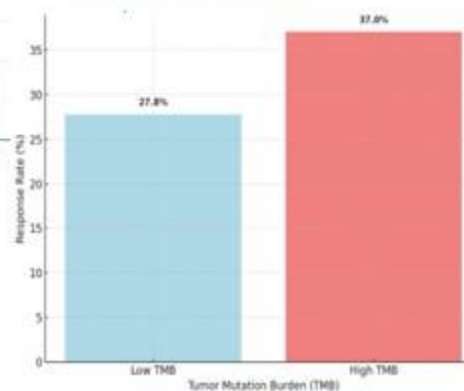


Table 4. Druggable genomic alteration analysis

An actionable alteration according to molecular tumor board ESCAT tier I criteria	21 patients
A potentially actionable alteration ESCAT tier II criteria	18 patients
Patients received targeted therapy based on MTB recommendation	7 (8%)

CONCLUSIONS

- Many patients with aUC harbour somatic pathogenic genomic alterations
- Patients with higher TMB have better response to ICI
- Integration of CGP in management of patients with aUC is feasible and yielded new therapeutic options in discernible proportion of patients with otherwise limited treatment options



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Table 1. Participating centers with submitted patients

KBC SESTRE MILOSRDNICE	53 (75)
OB PULA	7 (9)
KBC SPLIT	5 (6)
KBC OSIJEK	5 (6)
KBC ZAGREB	2 (2)
KLINIKA ZA TUMORE	2 (2)
TOTAL	74 (100%)

Table 2. Basic patient characteristics, N=74

age	66 (36-84)
primary tumor site	bladder 79%
site of metastasis	18% liver
ICI given in 1 st or 2 nd line	1 st line 68% 2 nd line 32%
ECOG 0 at the moment of NGS	59 (80%)
time NGS order-receipt of report	1 month
NGS of primary tumor, metastasis or blood	84% primary tumor 13% metastasis 2% blood
% of failed NGS	11% (N=8)
reasons for failed NGS	limited tissue 86%, tissue to old 12%

- A total of 229 genomic alterations were identified in 61 genes, median of 3 per patient
- Potentially actionable alteration was found in 39 (47%) patients
- Seven patients (8%) received targeted therapy: resulting in 2 cases of partial response, 3 stable disease and 2 progressive disease

1. NAGRADA

Klinički potencijal primjene Oncotype DX testa u liječenju ranog raka dojke u Hrvatskoj – prospektivna multicentrična studija

Mario Nalbalbani, Anuška Budisavljević, Renata Kelemenić-Dražin, Tajana Silovski, Marina Popović, Ivana Kukec, Martina Bašić Koretić, Eleonora Cini Tešar, Josipa Flam, Josipa Jović Zlatović, Filip Grubišić Čabo, Vesna Telesmanić Dobrić, Sara Bilić Knežević, Slavica Zubčić, Mislav Čonkas, Snježana Tomić, Marijana Jazvić, Natalija Dedić Plavetić

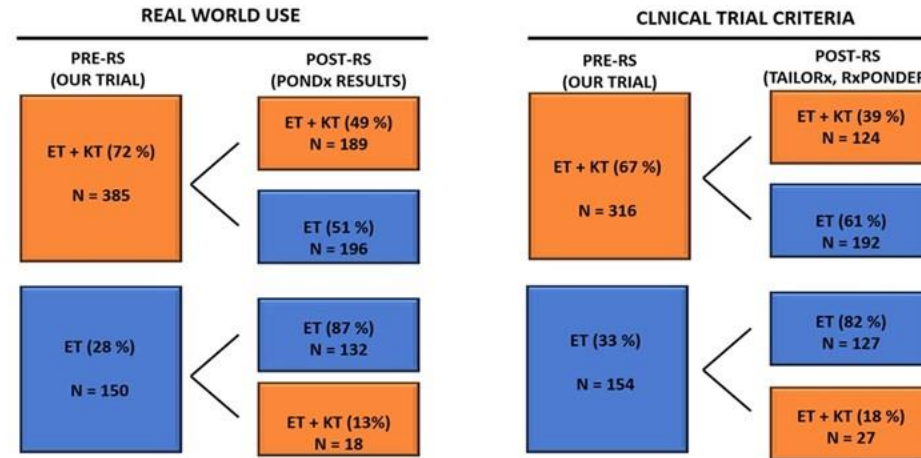
Possible clinical impact of implementing Oncotype DX test in treatment decision making for early breast cancer in Croatia - a prospective multicenter study

NALBANI M.¹, Budisavljević A.², Kelemenić-Dražin R.³, Silovski T.⁴, Popović M.⁴, Kuček I.⁴, Bašić Koretić M.⁵, Flam J.⁶, Cini Tešar E.⁷, Jazvić M.⁸, Jović Zlatović J.⁹, Grubišić-Čabo F.⁹, Telesmanić Dobrić V.¹⁰, Zubčić Krišto S.¹⁰, Bilić Knežević S.¹⁰, Čonkaš M.¹¹, Tomić S.¹², Dedić Plavetić N.⁴

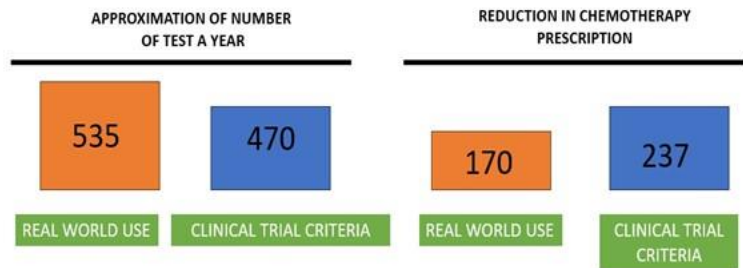
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INTRODUCTION: Deciding whether to use adjuvant chemotherapy in luminal breast cancers is challenging. The widespread use of Oncotype DX has simplified these decisions. Results from two clinical trials, **TAILORx** and **RxPONDER**, set the algorithm for interpreting Oncotype DX test results (1,2). Real-world data (**PONDx trial**) shows use of the Oncotype test results in 36% (49% deescalated, 13% escalated to chemotherapy) net reduction in chemotherapy prescription (3). Unfortunately, Oncotype is not covered by the Croatian Health Insurance Fund.

- METHODS:** Between April through June 2023., we conducted a prospective multicentric study in 10 out of 16 Croatian institutions with established oncology care.
- We recorded all newly diagnosed early luminal breast cancer patients and separately recorded candidates for Oncotype DX with their clinicopathological features.
- We used breast cancer incidence data from a Croatian Pathologist's Breast Cancer Working Group to make an approximation on the need for Oncotype use in one year.
- Finally, we made two simulations on the need and the effect of Oncotype use on the chemotherapy prescription: using real-world "broader" test inclusion criteria and interpretation of results, and more "strict" clinical trial inclusion criteria, and impact on chemotherapy prescription according to clinical trial results.



- CONCLUSION :** Multigenetic testing for adjuvant chemotherapy decision-making is an unmet need in Croatia.
- Using different criteria between 470 and 535 tests would be sufficient to cover the needs of the Croatian population.
- Testing should result in 170 to 237 fewer patients per year not receiving chemotherapy.
- Using strict clinical trial criteria and interpretation of results leads to a better impact index for Oncotype DX use. The financial impact will be further investigated.



- RESULTS:** We recorded 241 newly diagnosed luminal early breast cancer patients. Among them, 62 (25%) were eligible for Oncotype testing.
- In 2021, there were around 2140 newly diagnosed luminal early breast cancers, which means approximately 535 multigenetic tests per year would be prescribed in Croatia.
- In our study without Oncotype results, 45 (72%) patients were recommended chemotherapy. Using published real-world data (PONDx), this suggests that in one year, 170 patients could be spared chemotherapy.
- Using clinical trial criteria, 52 (21%) patients from our trial would be eligible for Oncotype, approximating the need for 470 annual tests. Using the published RS score distribution and clinical trial results (1, 2) on our trial population would result in 237 chemotherapy-less prescriptions a year.

IMPACT INDEX
DECREASE IN CHEMOTHERAPY PRESCRIPTION / NUMBER OF TEST

