BJMO clinic

Belgian Journal of Medical Oncology

VOLUME 15 | ISSUE 5
SEPTEMBER 2021

SPECIAL EDITION:

Highlights from ASCO 2021

VIRTUAL congress

Annual Meeting of the American Society of Clinical Oncology (ASCO)

June 4 - 8, 2021

5

THE BELGIAN JOURNAL OF MEDICAL ONCOLOGY IS THE OFFICIAL JOURNAL OF THE BELGIAN SOCIETY OF MEDICAL ONCOLOGY (BSMO) AND THE BELGIAN ASSOCIATION FOR CANCER RESEARCH (BACR)

COLOPHON

The Belgian Journal of Medical Oncology (BJMO) is the official scientific journal of the Belgian Society of Medical Oncology (BSMO) and the Belgian Association for Cancer Research (BACR). The BJMO aims to be a peer-reviewed cancer journal covering all aspects of the diagnostic and clinical management of cancer patients. Subscriptions are free for all specialists who are active in the fields of oncology, radiotherapy and adherent fields.

PUBLISHER AND EDITORIAL OFFICE
Ariez International B.V.
Ms. E. van Zanten, MSc
c/o Oude Houtlei 118-120, 9000 Gent, Belgium
Tel: 0031-75-642 94 20
E-mail: editor@bjmo.be

FOUNDED BY
L. Dirix, MD, PhD, medical oncologist, St Augustinus Hospital, Wilrijk.

EDITOR-IN-CHIEF
J. De Grève, MD, PhD, Professor in Oncology, head of department of medical oncology, University Hospital Brussels, Brussels.

EDITORIAL BOARD
A. Awada, MD, PhD, Professor in Oncology, Jules Bordet Institute, Brussels,
J-F. Baurain, MD, PhD, Professor in Oncology, Cliniques Universitaires Saint-Luc, Brussels,
F. Cornelis, MD, medical oncologist, Cliniques Universitaires Saint-Luc, Brussels,
H. Denys, MD, PhD, medical oncologist, University Hospital Gent, Gent,
M. De Ridder, MD, PhD, Professor in Radiation Oncology, UZ Brussel, Brussels,
M. Dicato, MD, haematologist-oncologist, Centre Hospitalier de Luxembourg, Luxembourg,
P. Dirix, MD, PhD, radiation oncologist, University Hospitals Leuven, Leuven,
L. Duck, MD, PhD, medical oncologist, Clinique Saint-Pierre, Ottignies,
C. Duhem, MD, haematologist-oncologist, Centre Hospitalier de Luxembourg, Luxembourg,
F. Duhoux, MD, PhD, medical oncologist, Cliniques Universitaires Saint-Luc, Brussels,
A. Hendrix, MD, medical oncologist, Gent University Hospital, Gent,
M. Ignatiadis, MD, PhD, medical oncologist, Jules Bordet Institute, Brussels,
G. Jerusalem, MD, PhD, medical oncologist, CHU Sart-Tilman, Liège,
J. Kerger, MD, PhD, medical oncologist, Jules Bordet Institute, Brussels,
J-P. Machiels, MD, PhD, Professor in Oncology, Cliniques Universitaires Saint-Luc, Brussels,
J. Mebis, MD, PhD, medical oncologist, Jessa Ziekenhuis, Hasselt,
P. Pauwels, MD, PhD, pathologist, University Hospital Antwerp, Edegem,
H. Prenen, MD, PhD, Professor in Oncology, University Hospitals Leuven, Leuven,
S. Rottey, MD, PhD, medical oncologist, Gent University Hospital, Gent,
D. Schrijvers, MD, PhD, medical oncologist, Ziekenhuisnetwerk Antwerpen, Antwerp,
P. Specenier, MD, PhD, Professor in Oncology, University Hospital Antwerp, Edegem,
J-L. Van Laethem, MD, PhD, Professor in Gastroenterology, Université Libre de Bruxelles, Brussels,
H. Van Poppel, MD, PhD, Professor in Urology, University Hospitals Leuven, Leuven,
D. Verhoeven, MD, PhD, medical oncologist, AZ KLINA, Brasschaat,
J.B. Vermorken, MD, PhD, Professor in Oncology, University Hospital Antwerp, Edegem,
H. Wildiers, MD, PhD, Professor in Oncology, University Hospitals Leuven, Leuven.

SUBSCRIPTIONS
For paid subscriptions, please refer to the publisher: abon@ariez.com.

Publication Frequency: 8 issues per year.
Edition: 3,000 copies.

COVER ILLUSTRATION
Science Photo

ISSN-NUMBER
1784-7141

BELGIAN JOURNAL OF MEDICAL ONCOLOGY

Highlights in gynaecological cancer

J.B. Vermorken, MD, PhD

"The United States is a long way from achieving clinical equity among its people" said Joe Elia, editor of NEJM Group in the introduction of the eBook on Racial Disparities in Clinical Medicine which was distributed among all ASCO members in June 2021. It is not without reason that this eBook is coming out now. In the President's Address, Lori J Pierce mentioned how segregation impacts on health care. "Today", she said, "ensuring equity of care – that is our good fight, this is the foundation of ASCO". It was interesting to notice that this topic also got attention in the Gynaecological Cancer track of the meeting. Overall, ASCO 2021 featured 14 presentations on cervical cancer, 32 on uterine cancer and 60 on ovarian cancer. The most important messages of these different presentations will be discussed in this article.
(BELG J MED ONCOL 2021;15(5):197-205)

CERVICAL CANCER

LOCALLY ADVANCED DISEASE

The most important information on the management of locally advanced cervical cancer (LA-CC) consisted of the OUTBACK trial, presented by *Dr. Mileshkin* from the Peter McCallum Center in Melbourne, during the plenary session of the meeting. Up to this very moment, the standard treatment for LA-CC has been concurrent chemoradiation (CCRT), mostly with low dose (40 mg/m^2) weekly cisplatin, and brachytherapy. Previous studies suggested that adjuvant chemotherapy (ACT) in addition to this standard approach might have a positive impact on survival.[1,2] However, these studies had limitations on their own, were not changing daily practice, and therefore a confirmatory trial was needed. OUTBACK is an international randomised phase III trial of the Gynecological Cancer InterGroup (GCIG).[3] Participating groups (countries) included ANZGOG (Australia and New Zealand), NRG (USA, Saudi Arabia, Canada, China) and Singapore. Eligible women had LA-CC suitable for CCRT with curative intent, FIGO 2008 stages IB plus positive lymph nodes, IB2, II, IIIB and IVA, ECOG performance status (PS) 0-2, tumours of squamous, adeno or adenosquamous cell type and no nodal disease above L3/4. Women were randomly assigned to either cisplatin-based standard CCRT or standard cisplatin-based CCRT followed by ACT with four cycles of paclitaxel (155 mg/m^2) and carboplatin (AUC5), after stratification for nodal status, participating site, FIGO stage, age and planned extended-field radiotherapy. Primary endpoint was overall survival (OS) at five years. Secondary endpoints presented at this meeting included, progression-free survival (PFS), adverse events (AE), patterns of disease recurrence and global health status and quality of life. From April 2011 to June 2017, 926 patients were accrued, of whom 919 were eligible, 463 in the ACT arm and 456 in the control arm. Median follow-up was 60 months. There was no survival benefit with ACT (OS 72% *vs.* 71%; PFS 63% *vs.* 61%) (*Figure 1*). The pattern of recurrence was similar and there was no decrease in distant metastases (9% *vs.* 11%). Toxicity (both haematologic and non-haematologic) was worse with ACT, but beyond one year, the only difference between arms consisted of an increased incidence of peripheral neuropathy (7% versus 2% grade 2 sensory) and there were no signs or

Department of Medical Oncology, Antwerp University Hospital, Edegem and Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium.

Please send all correspondence to: J. B. Vermorken, MD, PhD, Department of Medical Oncology, University Hospital Antwerp, Drie Eikenstraat 655, 2650 Edegem, Belgium, tel: +32 38214548, e-mail: JanB.Vermorken@uza.be.

Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.

Keywords: adavosertib, anlotinib, bevacizumab, bintrafusp alfa, BVAC-C, cemiplimab, cervical, chemoradiotherapy, gemogenovatucel-t, GX-188E, HRD, mirvetuximab soravtansine, neoadjuvant, ovarian cancer, PARP, pembrolizumab, pertuzumab, simlukafusp alfa, sintilimab, uterine cancer, vistusertib.

Highlights in breast cancer

J. Blokken, PharmD, PhD[1], T. Feys, MSc, MBA[1], K. Punie, MD[2], H. Wildiers, MD, PhD[2]

ASCO 2021 featured one crucial, practice-changing trial in early breast cancer: the OlympiA trial showed that one year of adjuvant olaparib improves invasive disease-free survival by 8.8% compared to placebo, when administered to high risk early breast patients (triple negative or hormone sensitive and HER2 negative) with a germline BRCA1 or 2 mutation. Furthermore, ECOG-ACRIN EA1131 failed to show improved outcome in triple negative breast cancer treated without pathological complete response after neoadjuvant chemotherapy with platinum based chemotherapy compared to the current standard capecitabine. GeparNUEVO for the first time showed long term outcome with anti-PD(L)1 therapy administered with neoadjuvant chemotherapy in triple negative breast cancer. In the advanced setting, interesting overall survival updates of the PALOMA-3 and MONALEESA-3 studies were presented. Furthermore, the SYsucc-002 trial demonstrated that trastuzumab plus endocrine therapy was non-inferior to and had fewer toxicities compared with trastuzumab plus chemotherapy in patients with HR+/HER2- metastatic breast cancer. In addition, this article will touch upon several other studies that are notable.
(BELG J MED ONCOL 2021;15(5):208-17)

EARLY BREAST CANCER

OLYMPIA: ADJUVANT OLAPARIB AFTER (NEO) ADJUVANT CHEMOTHERAPY

For patients with stage II/III *BRCA1/2*-associated breast cancer (BC), (neo)adjuvant chemotherapy ([N]ACT) is currently the standard of care. However, this treatment is associated with a substantial risk of recurrence. To improve on this, the phase III OlympiA trial investigates the potential of adjuvant olaparib (OL) in this setting since PARP inhibitors have shown to have high clinical activity in the metastatic setting in patients with *BRCA*1/2 mutations. In OlympiA, a total of 1,836 patients with HER2-negative early BC, who were either hormone receptor-positive (HR+) or triple negative (TNBC), were randomised (1:1) to receive either oral olaparib (300 mg twice daily) or placebo (PL) continuously for one year. Baseline demographics and tumour characteristics were well balanced between arms. At 36 months, the invasive disease-free survival (iDFS) in the intention-to-treat (ITT) population was reported at 85.9% and 77.1% with OL and PL, respectively (HR[95%CI]: 0.58[0.41-0.82], p< 0.0001). Overall, the number of iDFS events was lower in the OL arm, with 106 and 178 events occurring with OL and PL, respectively. Of note, most of these events consisted of distant recurrences (7.8% *vs.* 13.1%). With a longer follow-up of 3.5 years, results on iDFS supported the findings observed in the ITT population, with a three-year iDFS difference of 8.6% between OL and PL, with distinct and early curve separation (HR[99.5%CI]: 0.61[0.39-0.95]). Similar results were obtained in terms of distant disease-free survival (dDFS) at 36 months (87.5% *vs.* 80.4%, HR[99.5%-CI]: 0.57[0.39-0.83], p< 0.0001). Although OL was associated with a numerically higher three-year overall survival (OS) rate compared to PL, this difference was not statistically significant (92.0% *vs.* 88.3%, HR[99%]: 0.68[0.44-1.05], p= 0.024). Safety data were consistent with known side effects of olaparib, importantly with no excess serious adverse events or adverse events of special interest (like

[1]Ariez International, Ghent, Belgium, [2]University Hospital Leuven, Leuven, Belgium.
Please send all correspondence to: T. Feys, MSc, MBA, Ariez International, Oude Houtlei 118, 9000 Ghent, Belgium, tel: 0479 56 78 90, email: t.feys@ariez.com.
Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.
Keywords: ADAPT-HR-/HER2+, AMEERA-1, BEGONIA, breast cancer, DAWNA-1, DESTINY-Breast01, ECOG-ACRIN EA1131, FUTURE-CPLUS, GeparNuevo, IMpassion130, I-SPY2, MINDACT, MONALEESA-3, NEOTALA, NRG Oncology/NSABP B-42, OlympiA, PALOMA-3, PROMISE-GIM6, SYSUCC-002, TNBC.

Highlights in immunotherapy

B. Neyns, MD, PhD

Over the last decade immunotherapy has become an integral part of the oncogenic treatment arsenal. Meanwhile, the field of immune-oncology continues to evolve, which was amply illustrated by the large number of studies evaluating innovative immunotherapies presented at ASCO 2021.
(BELG J MED ONCOL 2021;15(5):218-23)

ANTI-LAG-3, A SUCCESSFUL COMBINATION PARTNER FOR ANTI-PD-1 THERAPY IN THE TREATMENT OF ADVANCED MELANOMA

LAG-3 (lymphocyte-activation gene 3) directed therapy moved to the forefront of melanoma immunotherapy at the 2021 annual ASCO meeting. The first planned analysis of the global, randomised, phase III RELATIVITY-047 trial (evaluating the outcome of 714 patients with previously untreated, unresectable metastatic melanoma who were randomly assigned 1:1 to receive every-four-week intravenous administration of relatlimab at 160 mg plus nivolumab at 480 mg or nivolumab 480 mg plus placebo, stratified by LAG-3 expression, PD-L1 expression, *BRAF* mutation status, and disease stage) indicated that patients who received relatlimab (an IgG4 anti-LAG-3 monoclonal antibody) in combination with nivolumab (an IgG4 anti-PD-1 mAB) resulted in a superior median progression-free survival of 10.1 months (significantly longer than that of patients who received nivolumab plus placebo; 4.6 months). After a median follow-up of 13.2 months, the study met its primary endpoint, with a hazard ratio of 0.75 and a p-value of 0.0055. As observed in other immune-checkpoint inhibitor studies, an early drop in the PFS curve occurred within the first six months but the PFS benefit from the combination therapy appeared early in the course of therapy (at the twelve weeks landmark). The combination was favoured across key prespecified subgroups. Treatment-related adverse events associated with relatlimab plus nivolumab were manageable. Although the incidence of grade 3 or 4 treatment-related adverse events was higher with the combination (18.9% *vs.* 9.7%), they occurred at a lower rate than we observe with the approved nivolumab plus ipilimumab combination. Treatment-related adverse events led to treatment discontinuation in 14.6% and 6.7% of patients receiving combination and monotherapy, respectively. There were three treatment-related deaths with the combination (haemophagocytic lymphohistiocytosis, acute oedema of the lung, and pneumonitis) and two with nivolumab monotherapy (sepsis/myocarditis and worsening pneumonia).[1] Forthcoming trial data (analysed according to trial design), including tumour response and overall survival rates, will further provide the community with additional data that will help to define the position of this new active immunotherapy regimen within the therapeutic landscape of unresectable advanced melanoma. Unanswered questions relate to the clinical benefit (risk/benefit) of this new combinatorial regimen as opposed to the activity of the approved ipilimumab plus nivolumab regimen and whether there is cross-resistance between both combination regimens. Adding to the enthusiasm regarding anti-LAG-3 therapy, were the results from a phase II trial investigating neoadjuvant nivolumab plus relatlimab. This small dual centre trial included 30 patients with surgically resectable clinical stage III or oligometastatic stage IV melanoma. The patients' median age was 60 years, 19 were men, and most (60%) had

Department of Medical Oncology, University Hospitals Brussels, Brussels, Belgium.
Please send all correspondence to: B. Neyns, MD, PhD, Department of Medical Oncology, University Hospitals Brussels, Laarbeeklaan 101, 1090 Jette, Belgium, tel: +32 24774111, email: bart.neyns@uzbrussel.be.
Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.
Keywords: adjuvant, afamitresgene autoleucel, BRAF, cemiplimab, checkmate-067, checkmate-511, checkmate-915, EORTC 1325, fianlimab, IMCgp100, immunotherapy, IOV-COM-202, ipilimumab, keynote-054, LAG-3, lifileucel, LN-144, melanoma, myxoid/round cell liposarcoma, neoadjuvant, nivolumab, PD-1, PD-L1, RELATIVITY-047, relatlimab, SPEARHEAD-1, synovial sarcoma, tebentafusp, V600E, V600K.

Highlights in head and neck cancer

W. Lybaert, MD

The ASCO Annual Meeting was held from 4 till 8 June 2021 in a virtual format. During this meeting, immunotherapy arrived in first-line recurrent/metastatic nasopharyngeal carcinoma, adjuvant capecitabine enters prudently the treatment algorithm of nasopharyngeal cancer, results of de-escalation studies in HPV-positive oropharyngeal cancer are promising and forwarding to phase III studies, cabozantinib shows impressive results in later-line radioiodine-refractory differentiated thyroid cancer, and immunotherapy tries to find a place in recurrent/metastatic salivary gland tumours, a tumour type without a uniform standard of care anno 2021. In this report, the most important headlines will be discussed, with comments on the clinical relevance of the different studies.
(BELG J MED ONCOL 2021;15(5):226-33)

IMMUNOTHERAPY ARRIVING IN FIRST-LINE RECURRENT/METASTATIC NASOPHARYNGEAL CARCINOMA

Anno 2021, the standard of care in first-line treatment for locally advanced/recurrent or metastatic nasopharyngeal carcinoma (NPC) is the combination chemotherapy gemcitabine + cisplatin. There are no approved therapies for later-line treatment of NPC, and **no immune checkpoint inhibitor has been approved for the treatment of NPC at this moment.**

STUDY 1: TORIPALIMAB + GEMCITABINE/CISPLATIN EXTENDS PROGRESSION-FREE SURVIVAL (PFS) IN RECURRENT OR METASTATIC NASOPHARYNGEAL CARCINOMA: JUPITER-02

Recently, the phase II clinical trial POLARIS-02 was published in the Journal of Clinical Oncology, with efficacy and safety results of toripalimab in previously treated recurrent or metastatic (R/M) NPC. Toripalimab is a humanised IgG4 monoclonal antibody against PD-1, already used in China for advanced melanoma and NPC in third-line. This study showed an overall response rate (ORR) of 20.5% with a median duration of response (DOR) of 12.8 months, median PFS 1.9 months and median OS 17.4 months. The POLARIS-02 study demonstrated a manageable safety profile and durable clinical response of toripalimab in patients with chemorefractory metastatic NPC. An early decrease in plasma EBV DNA copy number correlated with favourable response.[1]

At ASCO's Plenary Session, the results of JUPITER-02 were shown: a randomised, placebo-controlled, double-blinded phase III trial of toripalimab in combination with gemcitabine + cisplatin chemotherapy as first-line treatment for R/M NPC. Patients with advanced NPC with no prior chemotherapy in R/M setting were randomised (1:1) to receive toripalimab 240 mg or placebo d1 in combination with gemcitabine 1,000 mg/m2 d1+d8 and cisplatin 80 mg/m^2 d1 every three weeks (Q3W) for up to six cycles, followed by monotherapy toripalimab or placebo Q3W until disease progression, intolerable toxicity or completion two years of treatment. The primary endpoint was PFS by independent review committee (IRC) in the ITT population; secondary endpoints included ORR, DOR and OS. In total, 289 patients were randomised: 146 received toripalimab and 143 placebo. A significant improvement in PFS was seen for the toripalimab arm compared to the placebo arm (HR= 0.52, p= 0.0003), with median PFS 11.7 *vs.* 8.0 months. The one-year

Department of Medical Oncology, AZ Nikolaas, Sint-Niklaas, AZ Lokeren, Lokeren, AZ Sint- Augustinus, Antwerp, Belgium.
Please send all correspondence to: W. Lybaert, Department of Medical Oncology, AZ Nikolaas Hospital, Lodewijk De Meesterstraat 5, 9100 Sint-Niklaas, Belgium, email: willem.lybaert@aznikolaas.be.
Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.
Keywords: cabozantinib, camrelizumab, capecitabine, cetuximab, cisplatin, de-escalation, HNSCC, HPV-positive oropharyngeal cancer, immunotherapy, nasopharyngeal carcinoma, radiotherapy, salivary gland tumour, thyroid cancer, toripalimab,

Highlights in respiratory oncology

J. Blokken, PharmD, PhD, T. Feys, MSc, MBA

At ASCO 2021 much of the attention in the field of lung cancer went to early-stage non-small cell lung cancer (NSCLC) discussing both (neo)adjuvant strategies and local treatment modalities. In metastatic NSCLC, we would like to highlight some recent (chemo)immunotherapeutic advances in the treatment of non-oncogene addicted tumours as well as promising strategies to overcome osimertinib resistance, targeting of *KRAS* G12C mutated tumours and updated results for *EGFR* exon 20, *HER2* exon 20, *MET* and *RET* targeting. As a final abstract, the results of the randomised phase III CALGB 30610/RTOG 0538 trial evaluating high-dose thoracic radiotherapy in small cell lung cancer will be summarised. We would like to acknowledge *Prof. Veerle Surmont (University Hospital Ghent)* for her help in selecting the abstracts discussed in this overview.
(BELG J MED ONCOL 2021;15(5):237-44)

EARLY-STAGE NON-SMALL CELL LUNG CANCER

(NEO)ADJUVANT STRATEGIES

IMpower010 is a randomised phase III open-label trial comparing atezolizumab (sixteen cycles of 1,200 mg once every three weeks [Q3W]) to best supportive care (BSC) after surgery and adjuvant chemotherapy in patients with early-stage (IB-IIIA) NSCLC. The trial enrolled a total of 1,280 patients, of whom 1,269 received up to four 21-day cycles of adjuvant chemotherapy. All eligible patients had completely resected Stage IB (≥4 cm)-IIIA NSCLC (AJCC/UICC v7) and an ECOG performance status of 0-1. The primary endpoint of investigator-assessed disease-free survival (DFS) and secondary endpoint of overall survival (OS) were tested hierarchically.

After a median follow-up of 32.8 months, adjuvant atezolizumab was shown to induce a statistically significant DFS benefit over BSC in the population of patients with PD-L1 tumour cell [TC] ≥1% and Stage II-IIIA disease (median DFS not evaluable *vs.* 35.3 months, HR[95%CI]: 0.66[0.50-0.88], p= 0.004, *Figure 1*). This benefit was observed in all subgroups, except for active smokers at the time of enrolment and in patients harbouring an *ALK* rearrangement (both small subgroups of N= 75 and N= 23, respectively). Atezolizumab also reduced the risk of disease recurrence or death by 21% in all-randomised patients with stage II-IIIA NSCLC with a corresponding median DFS of 42.3 months compared to 35.3 months with BSC (HR[95%CI]: 0.79[0.64-0.96], p= 0.02). Interestingly, PD-L1 expression levels seem to be of clinical relevance in this trial, with a strong benefit for patients with tumour cell expression levels of at least 50% (HR[95%-CI]:0.43[0.27-0.66]) and no benefit for patients without PD-L1 expression (HR[95%CI]:0.97[0.72-1.31]). The statistical significance boundary was not crossed for atezolizumab *vs.* BSC for DFS in the ITT population (stage IB-IIIA NSCLC). OS data were still immature, and this endpoint was not formally tested at this interim analysis. Any-grade adverse events (AEs) occurred in 92.7% and 70.7% of patients in the atezolizumab and BSC groups, respectively. AEs were grade 3-4 in severity in 21.8% and 11.5% of patients, respectively. Grade 5 treatment-related AEs were rare and occurred in only 0.8% of patients in the atezolizumab arm. AEs leading to atezolizumab discontinuation were reported in 18.2% of atezolizumab-treated patients. Immune-mediated AEs mostly occurred in a small proportion of patients (<1%). However, grade 3/4 laboratory abnormalities for liver function were detected in 20 patients (4%) of which only four were diagnosed with hepatitis.

Ariez International, Ghent, Belgium.

Please send all correspondence to: T. Feys, MSc, MBA, Ariez International, Oude Houtlei 118, 9000 Ghent, Belgium, tel: 0479 56 78 90, email: t.feys@ariez.com.

Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.

Keywords: ARROW, CALGB 30610 (Alliance)/RTOG 0538, CheckMate 227, CheckMate 816, CheckMate 9LA, CodeBreaK100, CTONG1103, EXCLAIM, GEOMETRY mono-1, IFCT-1703 R2D2, IMPACT, IMpower010, NSCLC, PACIFIC, SCLC, STARS, VIOLET.

Highlights in gastro-intestinal cancers

J. Blokken, PharmD, PhD, T. Feys, MSc, MBA

At ASCO 2021, the most important studies in gastro-intestinal (GI) cancer related to the use of immunotherapy in cancers of the upper gastro-intestinal tract. For advanced oesophageal squamous cell carcinoma (ESCC), the CheckMate 648 trial demonstrated that both nivolumab plus chemotherapy and nivolumab plus ipilimumab represent a new potential first-line standard of care, especially for patients with a tumour PD-L1 expression of at least 1%. For adenocarcinoma of the oesophagus and oesophago-gastric junction, there is no evidence that peri-operative chemotherapy is unacceptably inferior to multimodal therapy. For tumours of the lower gastro-intestinal tract, the most important results came from the DESTINY-CRC01, CHRONOS, FIRE-4.5 and PANAMA studies.
(BELG J MED ONCOL 2021;15(5):248-53)

UPPER GASTRO-INTESTINAL TRACT

OESOPHAGEAL SQUAMOUS CELL CARCINOMA

In the phase III CheckMate 648 study, 970 patients with previously untreated, unresectable, advanced oesophageal squamous cell carcinoma (ESCC) were recruited, irrespective of their tumour PD-L1 expression levels. Patients were randomly allocated (1:1:1) into three groups. Group 1 assessed the addition of 240 mg nivolumab (NIVO) once every two weeks (Q2W) to chemotherapy (fluorouracil + cisplatin) Q4W while Group 2 is a chemotherapy-free treatment option of NIVO 3mg/kg Q2W + ipilimumab (IPI) 1mg/kg Q6W. Finally, Group 3 is a control arm in which patients received chemotherapy Q4W alone. Primary endpoints for both comparisons are overall survival (OS) and progression-free survival (PFS) per blinded independent central review (BICR) in patients with a tumour PD-L1 expression level of at least 1%. At the time of the presented analysis, patients were followed-up for a minimum of 12.9 months. For the first comparison of NIVO + chemo *vs.* chemo alone, a highly statistically significant improvement in OS was observed in patients with tumour cell PD-L1 ≥1% (*Figure 1A*). The median OS was 15.4 months for patients treated with NIVO + chemo and 9.1 months for patients receiving chemo alone (HR[99.5%CI]: 0.54[0.37-0.80], p< 0.0001). A similar trend was observed among the all randomised patient population with a median OS of 13.2 and 10.7 months, respectively (HR[99.1%CI]: 0.74[0.58-0.96], p= 0.0021). In addition, also the PFS was significantly improved in the primary patient population of PD-L1 ≥1% (HR[95%CI]: 0.65[0.46-0.92], p= 0.0023). However, this was not the case in all randomised patients (HR[95%CI]: 0.81[0.64-1.04], p= 0.0355). The objective response rates (ORR) with NIVO + chemo was 53% *vs.* 20% with chemotherapy alone in patients with PD-L1 ≥1% (47% *vs.* 27% in all randomised patients). Also for the second comparison of NIVO + IPI *vs.* chemo, a significant OS advantage was seen in favour of the immunotherapy-based regimen in the primary study population (13.7 *vs.* 9.1 months, HR[98.6%CI]: 0.64[0.46-0.90], p= 0.0010, *Figure 1B*). This was also the case when looking at the entire randomised patient population (12.8 *vs.* 10.7 months, HR[98.2%CI]: 0.78[0.62-0.98], p= 0.0110). The primary endpoint of PFS per BICR was not met in patients with tumour cell PD-L1 ≥1% (HR[95%CI]: 1.02[0.73-1.43], p= 0.8958) nor was this the case in all randomised patients (HR[95%CI]: 1.26[1.04-1.52], p-value not tested). ORR with NIVO + IPI and chemotherapy were 35% and 20%, respec-

Ariez International, Ghent, Belgium.

Please send all correspondence to: T. Feys, MSc, MBA, Ariez International, Oude Houtlei 118, 9000 Ghent, Belgium, tel: 0479 56 78 90, email: t.feys@ariez.com.

Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.

Keywords: Biliary tract, CheckMate 577, CheckMate 648, CHRONOS, colorectal cancer, DESTINY-CRC01, ESCORT-1, FIRE-4.5, FOCUS4-N, gastro-intestinal, gastro-oesophageal junction, Neo-AEGIS, NIFTY, PANAMA, TRUSTY.

Highlights in genitourinary cancers

T. Vermassen, PhD[1,2], S. Rottey, MD, PhD[1,2], D. De Maeseneer, MD[1,3]

The 2021 ASCO Annual Meeting offered a variety of advancements in the treatment and detection of genitourinary cancers. For prostate cancer (PCa), matched tumour-normal tissue sequencing was shown to be the ideal standard of care (SOC) in *de novo* high-risk PCa patients. The addition of immune checkpoint inhibitors (ICI) to the SOC was found to be highly effective in muscle-invasive bladder cancer, with enfortumab vedotin (EV) continuing to show efficacy in urothelial carcinoma in a post-ICI advanced/ metastatic setting. Finally, the combination of ICI and tyrosine kinase inhibitors (TKIs) as first-line therapy for both non-clear cell and clear cell renal cell carcinoma (non-cc/ccRCC) displays a clear survival benefit, with this efficacy extending into the second-line treatment of patients with metastatic non-ccRCC who have previously received ICIs. The most important headline presentations relating to genitourinary cancers will be discussed in this congress highlights article.

(BELG J MED ONCOL 2021;15(5):256-63)

PROSTATE CARCINOMA

FINDINGS ON PROSTATE CANCER (PCa) TUMOUR SEQUENCING – SUBSEQUENT NEED FOR GERMLINE TESTING?

Tumour sequencing is increasingly being used for therapeutic selection in men with advanced PCa. In case of tumour-only sequencing, identified mutations can either be somatic or germline in origin. The objective of this study was to determine the overall and gene-specific probability of pathogenic/likely pathogenic germline mutations. Targeted next-generation sequencing of PCa tumour and matched peripheral blood was performed in 1,883 men (84% high-risk PCa, 52% metastatic PCa [mPCa], 38% family history). A total of 19% of patients had at least one (somatic or germline) mutation and germline mutations were found in 10% of patients. The average germline probability was 40%, with highest probabilities for *CHEK2* (83%), *PALB2* (69%), *HOXB13* (60%), *BRCA1* (55%) and *BRCA2* (47%). These mutations would not have been reported as germline without matched normal and 46% would not have been detected based on family history. As such, men undergoing tumour-only sequencing should be counselled on the possibility of uncovering possible pathogenic germline mutations.[1]

ERASE: NEED FOR PHYSICAL EXERCISE DURING ACTIVE SURVEILLANCE

Men with PCa undergoing active surveillance are at an increased risk of cardiovascular death and disease progression. To address this, the phase II randomised controlled ERASE trial investigated the effects of exercise on cardiorespiratory fitness and biochemical progress of PCa. A total of 52 men with localised PCa on active surveillance were randomised (1:1) to high-intensity interval training (HIIT, supervised aerobic HIIT on a treadmill at 85-95% of peak cardiorespiratory fitness thrice-weekly for twelve weeks) or usual care. The outcomes were cardiorespiratory fitness, biochemical progression of PCa and prostate-specific antigen (PSA) kinetics. Forty-six participants completed the trial and adherence to HIIT was 96%. Compared to usual care, HIIT significantly improved cardiorespiratory fitness (mean

[1]Department Medical Oncology, University Hospital Ghent, Ghent, Belgium, [2]Drug Research Unit Ghent, University Hospital Ghent, Ghent, Belgium, [3]Department of Medical Oncology, AZ Sint-Lucas, Bruges, Belgium.

Please send all correspondence to: S. Rottey, MD, PhD, Department for Medical Oncology, University Hospital Ghent, C. Heymanslaan 10, 9000 Ghent, Belgium, email: Sylvie.Rottey@UGent.be.

Conflict of interest: The selection of the abstracts discussed in this overview was not influenced by third parties.

Keywords: abiraterone, axitinib, cabozantinib, enfortumab vedotin, enzalutamide, ERASE, immunotherapy, nivolumab, PEACE-1, pembrolizumab, prostate cancer, renal cell carcinoma, STAMPEDE, targeted therapy, urothelial carcinoma.

New oncology reimbursements in Belgium

T. Feys, MBA, MSc, J. Blokken, PharmD, PhD

OVERVIEW OF BELGIAN REIMBURSEMENT NEWS

(BELG J MED ONCOL 2021;15(5):264-5)

TALAZOPARIB (TALZENNA®)

Since July 1st, 2021, the PARP inhibitor talazoparib is reimbursed as monotherapy for the treatment of adult patients with a germline *BRCA*1/2 mutation having locally advanced, unresectable, or metastatic triple negative (TNBC) or hormone-receptor positive/HER2-negative breast cancer. Talazoparib is reimbursed in the first, second or later treatment line in the advanced breast cancer setting. In order to be eligible for reimbursement, the patient has to be previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced, or metastatic setting unless the patients is considered to be unsuitable for this treatment. In case of HR-positive breast cancer, the patient has to be pre-treated with hormone therapy, or should be unsuitable for this treatment modality. Importantly, the presence of a germline *BRCA* mutation needs to be confirmed by an accredited centre for medical genetics.

The reimbursement of talazoparib in this setting is based on the results of the randomised, phase III EMBRACA trial.[1] In this trial, a total of 431 patients with advanced breast cancer and a germline *BRCA*1/2 mutation were assigned (2:1) to receive talazoparib (1 mg once daily) or standard single-agent therapy of the physician's choice (capecitabine, eribulin, gemcitabine, or vinorelbine in continuous 21-day cycles). Talazoparib was found to be associated with a significantly better progression-free survival with a median of 8.6 months as compared to 5.6 months in the control arm (HR[95%CI]: 0.54[0.41-0.71]; p< 0.001). Also the objective response rate was significantly higher with talazoparib than with the control regimen at 62.6% and 27.2%, respectively (OR[95%-CI]: 5.0[2.9-8.8]; p< 0.001). The PFS benefit seen with talazoparib did not translate in a significantly better overall survival, although this analysis was probably influenced by the use of subsequent treatments.[2] Finally, patient reported outcomes with talazoparib were superior to what was seen in the control arm.[1]

CEMIPLIMAB (LIBTAYO®)

Cemiplimab (Libtayo®) was already reimbursed as monotherapy for the treatment of patients with locally advanced or metastatic cutaneous squamous cell carcinoma. Since July 1st 2021, the Belgian reimbursement criteria for this human monoclonal anti-PD1 antibody were broadened. The agent is now also eligible for reimbursement as first line therapy for adult patients with non-small cell cancer (NSCLC) having a PD-L1 expression in at least 50% of tumour cells and who are not harbouring a mutation in *EGFR*, *ALK*, or *ROS*. In order to be eligible for reimbursement, patients have to have locally advanced disease without the option for definitive chemoradiotherapy or have metastatic NSCLC. The reimbursement of cemiplimab in NSCLC is based on the results of the EMPOWER-Lung 1 trial in which cemiplimab was found to significantly improve the over-

Ariez International BV, Ghent, Belgium.

Please send all correspondence to: T. Feys, MBA, MSc, Ariez International BV, Oude Houtlei 108A, 9000 Ghent, Belgium, tel: +32 (0)479 56 78 90, email: t.feys@ariez.com.

Conflict of interest: The content of this article was not influenced by third parties and is the sole responsibility of the editor.

Keywords: apalutamide, cemiplimab, Erleada®, Libtayo®, Talzenna®, talazoparib.

INTERNATIONAL & NATIONAL CONGRESSES 2020

Virtual - ESHNR 2021
2-4 September 2021

Virtual - ILCA 2021 – The International Liver Cancer Association's 15th Annual Conference
2-5 September 2021

AUA 2021 Annual Meeting
10-13 September 2021
Las Vegas, NV, United States

IASLC 2021 World Conference on Lung Cancer
8-14 September 2021
Denver, CO, United States

Virtual - ESMO Congress 2021
16-21 September 2021

21st SIS World Congress on Breast Cancer and Breast Healthcare
22-25 September 2021
Rhodes Island, Greece

Virtual - EANO 2021 Meeting
25-26 September 2021

ASCO Quality Care Symposium
24-25 September 2021
Boston, MA, United States and online

30th EADV Congress
29 September -2 October 2021
Vienna, Austria

MSTS Annual Meeting
6-8 October 2021
Baltimore, MD, United States