

INTEGRATING SCIENCE INTO ONCOLOGY FOR A BETTER PATIENT OUTCOME

DAILY REPORTER

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Practice-changing phase III data in melanoma patients cause excitement at a Presidential Symposium



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Late-Breaking Abstract presentations of phase III trial data in yesterday's Presidential Symposium gave exciting new insights into the future of treatment for resected, high-risk melanoma.

One of two studies investigating adjuvant BRAF inhibitor therapy for patients with *BRAF*V600 mutation-positive melanoma, the COMBI-AD trial, reported that the combination of dabrafenib plus trametinib significantly doubled relapse-free survival (RFS)—the primary endpoint—and improved a number of other endpoints, such as overall survival (OS), distant metastasis-free survival and freedom from relapse, compared with placebo in 870 patients with stage III disease (Abstract LBA6_PR).¹ In the placebo-controlled BRIM8 trial, disease-free survival benefits with vemurafenib were substantial and significant for stage IIC–IIIB melanoma, but did not reach significance for stage IIIC disease (Abstract LBA7_PR).

During the same session, the CheckMate 238 trial demonstrated that adjuvant nivolumab was more effective than ipilimumab among 906 patients with stage III/IV melanoma after complete resection (Abstract LBA8_PR).² The trial was stopped early due to clear evidence of benefit with nivolumab, which not only significantly improved RFS (hazard ratio [HR] 0.65; $p < 0.0001$), but was far better tolerated.

The separate findings that combination dabrafenib–trametinib and nivolumab monotherapy have demonstrated survival benefits in the stage III melanoma setting will undoubtedly be practice changing.

Professor Georgina Long from Melanoma Institute Australia, Sydney, Australia, commented, “These results are a game changer for the way we manage high-risk resected melanoma. The reduction in risk of recurrence of 35% for adjuvant nivolumab versus ipilimumab, and 53% for dabrafenib plus trametinib versus placebo, were highly significant and are clinically meaningful. Also, we saw an OS benefit with dabrafenib and trametinib, with a 43% reduction in the risk of death.”

1. Long GV, et al. N Engl J Med 2017. Sept 10. Epub ahead of print
2. Weber J, et al. N Engl J Med 2017. Sept 10. Epub ahead of print



View the ESMO 2017 Broadcast on the YouTube playlist here.



ESMO 2017: *Daily Reporter* Editorial Team highlights



Left to right: Angela Lamarca (The Christie NHS Foundation Trust, Manchester, UK); Markus Joerger (St. Gallen Cancer Centre, Switzerland); Evandro de Azambuja (Jules Bordet Institute, Brussels, Belgium); Floriana Morgillo (University of Campania "Luigi Vanvitelli", Caserta, Italy); Stefan Zimmermann (Lausanne University Hospital, Switzerland); Rodrigo Dienstmann (Vall d'Hebron Institute of Oncology, Barcelona, Spain); Giuseppe Curigliano (European Institute of Oncology, Milan, Italy).

As the Congress draws to a close, we have taken time to briefly escape to the quiet of the *Daily Reporter* office to pull together some of our thoughts on the greatest hits of ESMO 2017. We feel energised by the scale and the volume of extraordinary new findings and advances across different cancer types. The team have been particularly hard-pressed this Congress to select just the few abstracts we feel represent a significant advance in managing cancer and that reflect the collaborative and reciprocal science-clinic relationship, which is what will drive forward the process of finding new and better treatments for patients.

Giuseppe Curigliano (Editor-in-Chief) and Evandro de Azambuja (Associate Editor): As we race ahead with new innovations we should also remember that it is not only new that is good, it is how we combine new innovations and existing treatments that may provide us with the answers to some of the remaining questions. For this reason we have chosen as one of our top picks for breast cancer the phase II TOPIC trial, which investigated radiotherapy (RT) or low-dose chemotherapy prior to treatment with nivolumab in patients with metastatic triple-negative disease (Abstract LBA14). What this non-comparative trial showed was that using the established modality of RT as induction therapy prior to treatment with the more innovative approach of immune checkpoint inhibition led to a durable partial response in 1 of 10 patients, with responses lasting almost 1 year. In addition, patients receiving low-dose doxorubicin achieved response rates of around 45%. We also think that the exciting data from the phase III MONARCH 3 trial

should be highlighted, as they strengthen confidence in the use of CDK4/6 inhibitors for the first-line treatment of hormone receptor-positive HER2-negative advanced/metastatic breast cancer (Abstract 2360_PR). When combined with anastrozole or letrozole, the CDK 4/6 inhibitor abemaciclib significantly prolonged progression-free survival (PFS) compared with placebo (not reached versus 14.7 months; hazard ratio [HR] 0.543; $p=0.00021$). There was a suggestion from exploratory analyses that this regimen was most suitable for patients with indicators of poor prognosis, while endocrine therapy alone produced excellent outcomes in patients with bone-only disease.

Markus Joerger (Associate Editor): ESMO 2017 has once again featured a number of potentially practice-changing study presentations, prime among them for urogenital cancers being CheckMate 214 in treatment-naïve patients with metastatic or advanced renal cell carcinoma (Abstract LBA5). In this phase III study, first-line immunotherapy (nivolumab plus ipilimumab) led to a 37% reduction in the risk of death compared with sunitinib, the current standard of care anti-angiogenic tyrosine kinase inhibitor (median overall survival [OS] not reached versus 26.0 months; $p<0.0001$). No less important for patients were the findings that the immunotherapy arm was associated with fewer grade 3–5 treatment-related adverse events (46% versus 63%) and that patients appeared to have a better quality of life (QoL) with improved symptom control. It is likely that these results will herald the combination of nivolumab and ipilimumab as the new first-line standard of care for these patients.

Stefan Zimmermann (Associate Editor): The results of the phase III PACIFIC trial are hugely significant for the treatment of patients with locally advanced, unresectable non-small-cell lung cancer (NSCLC; Abstract LBA1_PR).¹ The finding that consolidation with the PD-L1-targeting agent durvalumab following platinum-based chemoradiotherapy markedly and significantly improved PFS compared with placebo (16.8 months versus 5.6 months; $p<0.0001$) shows that we are harnessing something extraordinary with the use of immunotherapy in this setting. Without a doubt, one of the most important take-

home messages for NSCLC comes from studies in ALK-positive disease. In the phase III ALEX study, alectinib showed superior CNS activity to crizotinib in untreated ALK-positive NSCLC (12-month cumulative incidence of CNS progression: 16.0% versus 58.3%; $p<0.0001$; Abstract 12980_PR). Patients with ALK-positive NSCLC commonly have brain metastases prior to treatment and the extended OS times we are achieving with improved management approaches are accompanied by an increasing frequency of subsequent brain metastases.

The key issue here is that we need to target brain metastases at the start of treatment and with the strongest weapons.

Also, if there were any remaining doubts regarding the optimal sequencing of targeted therapies in advanced NSCLC after the presentation of the FLAURA trial (Abstract LBA2_PR), we should learn from the ALK-positive NSCLC experience that patient attrition following first-line treatment means that they may not be around to benefit from second-line therapy.

Floriana Morgillo (Associate Editor): ESMO 2017 has been a great congress for progress in melanoma, particularly in patients with high-risk locally advanced disease. Phase III COMBI-AD (Abstract LBA6_PR) and BRIM8 (Abstract LBA7_PR) trials revealed substantial clinical benefit for adjuvant BRAF inhibitor therapy in patients with *BRAF*V600-mutated melanoma. Combination dabrafenib plus trametinib more than doubled relapse-free survival (RFS) compared with placebo, while in the BRIM8 trial, adjuvant vemurafenib significantly improved disease-free survival (DFS) in patients with stage IIC–IIIB disease. The phase III CheckMate 238 study of adjuvant nivolumab after complete resection in patients with stage III/IV melanoma was stopped early because it showed a clear benefit

in terms of RFS compared with ipilimumab (HR 0.65; $p<0.0001$), and was much better tolerated; 10% of patients stopped taking nivolumab due to side effects compared with 43% taking ipilimumab (Abstract LBA8_PR). Promising data were also presented for combined therapy with anti-lymphocyte activation gene-3 (LAG-3) monoclonal antibody plus nivolumab in heavily pre-treated patients who had progressed on PD-L1/PD-1 therapy (Abstract LBA18). The hope is that simultaneous blockade of LAG-3 and PD-1 may synergistically restore T-cell activation and enhance antitumour immunity. At ESMO 2016, ipilimumab was at the forefront of a new wave of agents bringing significant benefits in terms of PFS and OS to patients with stage III melanoma for whom there is currently no standard of care. However, these benefits were overshadowed by high toxicity. Ipilimumab is the standard of care in the USA, but this is not the case in Europe, and the ESMO 2017 results are therefore very welcome news for patients with advanced stage melanoma.

Angela Lamarca (Associate Editor): For me, data from biomarker and QoL analyses of the phase III study that demonstrated non-inferiority between first-line lenvatinib and sorafenib provide important information on a potential new treatment option for patients with unresectable hepatocellular carcinoma. The identification of potential serum biomarkers and gene expression levels, as reported in Abstract LBA30, are an important step in helping to guide treatment and will be critical to the optimal use of lenvatinib in the clinic. Results of the QoL analysis indicated that while there was in general non-inferiority between lenvatinib and sorafenib, there was evidence of some significant health-related QoL benefits with lenvatinib for several domains, including diarrhoea, pain and nutrition (Abstract 6180).

These findings will help to guide clinicians’ decisions regarding personalised treatment for each patient.

It was also really exciting to see data indicating that neuroendocrine tumours are now taking their first steps into the worlds of precision medicine (Abstracts 4300 and 4310) and immunotherapy (Abstracts 4270 and 4280).

Rodrigo Dienstmann (Associate Editor): My choice of top pick has to be the updated results and panel discussion of the unprecedented IDEA collaboration in early-stage colorectal cancer, with a pooled analysis of six clinical trials including more than 12,000 patients. Clinicians left the room with a clear message on the duration of adjuvant chemotherapy: for the CAPOX regimen, 3 months is non-inferior to 6 months; for the FOLFOX regimen, 3 months is inferior to 6 months. Sub-group analysis shows that there remains uncertainty on the treatment duration for patients with pT4 or pN2 tumours and experts favoured CAPOX or FOLFOX for 6 months, particularly for patients willing to fight for a potential 2% absolute gain in 3-year DFS. Most importantly, 3 months’ adjuvant treatment duration led to a 2–4-fold reduction in the risk of diarrhoea, mucositis, hand–foot syndrome and long-term neurotoxicity.

We want to close this editorial by thanking: our two new team members, Rodrigo Dienstmann and Angela Lamarca, both of whom have thoroughly enjoyed the

experience; all the contributors, for making the *Daily Reporter* such an interesting and integral part of ESMO 2017; and, of course, you the readers, for sharing our journey through the Congress.

We look forward to seeing you again at ESMO 2018 in Munich, Germany (19–23 October)!

1. Antonia SJ, et al. N Engl J Med 2017. Sept 8. Epub ahead of print

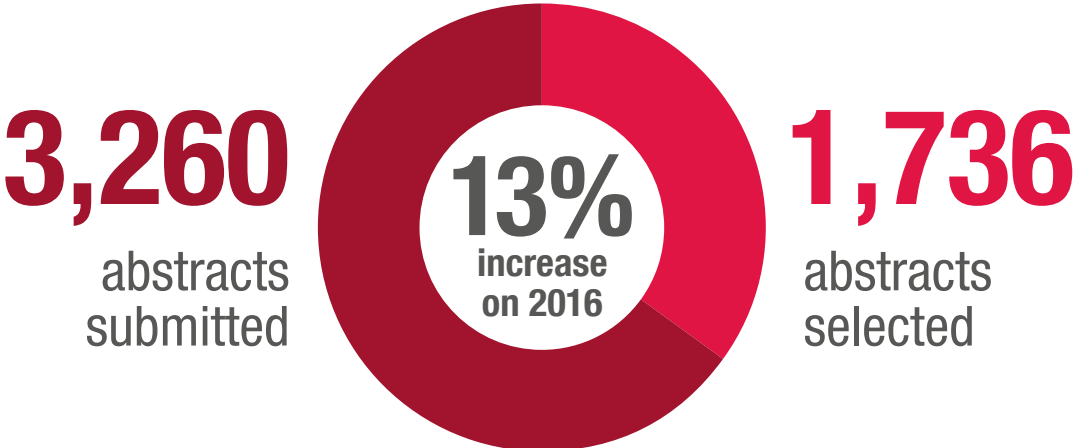
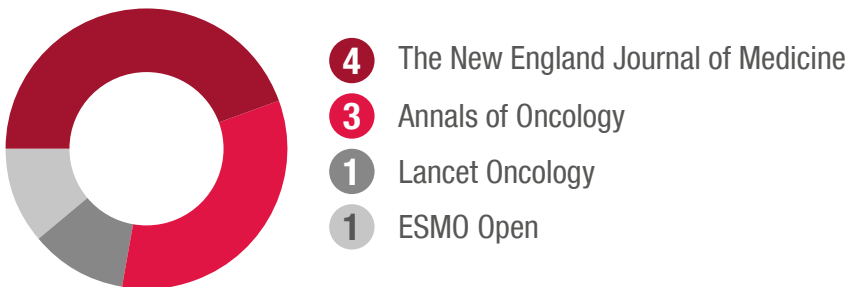
ESMO would like to thank the *Daily Reporter* Editorial Team, Editor-in-Chief Giuseppe Curigliano and the Associate Editors Evandro de Azambuja, Rodrigo Dienstmann, Markus Joerger, Angela Lamarca, Floriana Morgillo and Stefan Zimmermann, together with TMC Strategic Communications, for their dedication in bringing you all the important news from ESMO 2017. We think you will agree that the team did an amazing job of reflecting the theme of the Congress in their articles and reports and in representing the wide variety of sessions taking place at the meeting. Congratulations on another successful year!



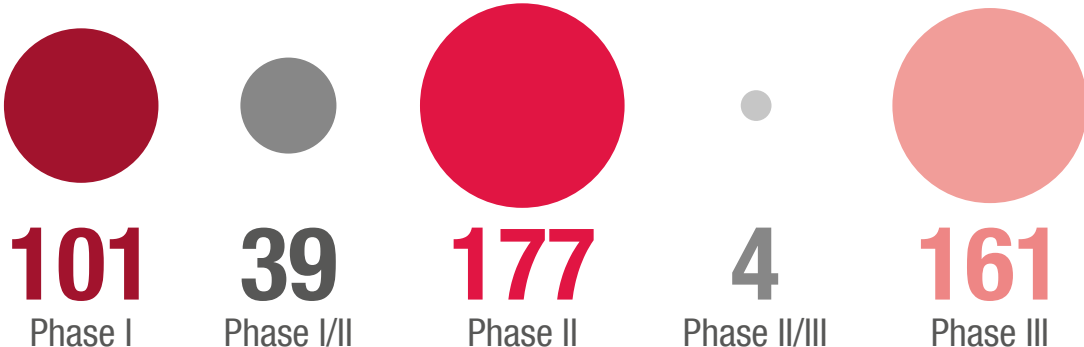
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SIMULTANEOUS PUBLICATIONS



CLINICAL TRIALS REPRESENTED



Antitumour activity for novel small molecules targeting rare mutations in NSCLC

A growing understanding of the pathobiology of non-small-cell lung cancer (NSCLC) has revealed a number of genetic mutations that act as oncogenic drivers of disease progression and can be targeted by therapeutic small molecules. Earlier this week, investigators from Institut Gustave Roussy, Villejuif, France, presented data from two phase II studies investigating the clinical activity of novel small molecules in patients with NSCLC characterised by rare mutations.

Substantial clinical activity was previously demonstrated with combined BRAF (dabrafenib) plus MEK (trametinib) inhibition in a pre-treated patient cohort from a phase II trial (BRF113928) of *BRAF*V600E-mutant metastatic NSCLC: 67% objective response rate (ORR), 10.2 months median progression-free survival (PFS), and 18.2 months median overall survival (OS).¹ In a Late-Breaking Abstract presentation yesterday (Abstract LBA51), Dr David Planchard reviewed data from a cohort of 36 patients from the same trial with previously untreated *BRAF*V600E-mutant NSCLC who received first-line dabrafenib plus trametinib. The ORR, median PFS and OS were 64%, 10.9 months and 24.6 months, respectively. The combination had a manageable safety profile that was similar to previous experience, with no new safety signals observed.

Substantial antitumour activity was observed in treatment-naïve patients, with an investigator-assessed confirmed ORR (primary endpoint) of 64%, including two complete responses.

Commenting on the findings, Dr Planchard said, “This study represents the first evaluation, to our knowledge, of combined BRAF and MEK inhibition in patients with previously untreated NSCLC.” Based on these results, and the data reported in pre-treated patients,¹ dabrafenib plus trametinib was recently approved by the European Commission and US FDA for patients with *BRAF*V600E-mutant NSCLC, regardless of prior treatment history.

On Sunday, Dr Benjamin Besse (Abstract 1308PD) discussed the findings of an ongoing study of lorlatinib, a molecule known to penetrate the blood–brain barrier, in 47 patients with *ROS1*-rearranged NSCLC. Most patients (72%) had received prior crizotinib (n=34) and 53% (n=25) had CNS involvement. Clinical activity was demonstrated, with an ORR of 36.2% and an intracranial ORR of 56.0%, and the treatment was well tolerated.

Outcomes for patients with NSCLC have already improved in recent times and as individualised treatment algorithms continue to be refined, we can expect to see even greater advances in this setting.

1. Planchard D, et al. J Clin Oncol 2017;35(Suppl):9075



Survival benefit suggested with pembrolizumab in HNSCC: Final analysis of KEYNOTE-040

Pembrolizumab has demonstrated a trend towards improved overall survival (OS) compared with standard of care (SoC) chemotherapy in 495 patients with relapsed/metastatic head and neck squamous cell carcinoma (HNSCC). In a Late-Breaking Abstract presentation yesterday (Abstract LBA45_PR), Dr Ezra Cohen from the San Diego Moores Cancer Center, La Jolla, CA, USA, noted a 19% reduction in risk of death with pembrolizumab compared with SoC in a final analysis of the phase III KEYNOTE-040 trial.

However, at a median follow-up of 7.3 months, the OS difference in the intent-to-treat population (hazard ratio 0.81; p=0.0204) did not reach statistical significance according to a pre-specified efficacy boundary of p=0.0175. Commenting on the data, Dr Cohen pointed out that 12.5% of patients in the SoC arm subsequently received immunotherapy, and this may have confounded the analysis.

Patients with advanced HNSCC experienced improved survival with pembrolizumab compared with SoC chemotherapy; this benefit was substantial in PD-L1-positive tumours.

A substantially lower rate of grade 3–5 adverse events was reported with pembrolizumab than with SoC: 13.4% versus 36.3%, respectively.

Commenting on the findings, trial investigator Professor Jean-Pascal Machiels from Institut Roi Albert II, Cliniques Universitaires Saint-Luc, Brussels, Belgium, said, “Although the study did not meet its primary endpoint, the data are consistent with other trials and support the activity of PD-1/PD-L1 inhibitors in patients with HNSCC who progress after platinum therapy. Some patients derived long-term benefit with anti-PD-1 therapy, and this has never been observed before. Today, the challenges are to identify biomarkers and to integrate anti-PD-1 agents within earlier treatment lines.”



Robust intracranial activity with alectinib in NSCLC with CNS involvement

More than 20% of patients with non-small-cell lung cancer (NSCLC) have brain metastases (BM) at diagnosis, with a substantial proportion developing BM at some stage of the disease.¹ According to the results of an online survey of EU societies involved in the treatment of lung cancer patients, management of BM varies considerably (Abstract 1372P).

Only one-third of clinicians used prognostic classification to guide therapeutic decisions in patients with BM.

In patients with *ALK*-positive NSCLC, the cumulative lifetime incidence of BM is as high as 70%.² Crizotinib has been the standard of care in this setting, but CNS disease—the dominant site of progression on crizotinib—is frequently observed within a year.³ Newer *ALK* inhibitors, such as alectinib, have been developed to provide additional treatment options.

A Proffered Paper Session yesterday included impressive data from two phase III trials of alectinib in *ALK*-positive NSCLC with CNS

involvement. In the ALEX study, alectinib significantly reduced the 12-month cumulative incidence of CNS progression compared with crizotinib (16.0% versus 58.3%; p<0.0001) and increased the CNS objective response rate (ORR) among 122 treatment-naïve patients; improvements were significant regardless of prior radiotherapy use (Abstract 12980_PR). In the ALUR study in 107 patients previously treated with both platinum-based chemotherapy and crizotinib, alectinib significantly reduced the risk of investigator-assessed disease progression compared with standard relapse therapy (hazard ratio 0.15; 95% confidence interval 0.08–0.29; p<0.001) and improved the CNS ORR (54.2% versus 0%; Abstract 12990_PR). Enhanced systemic and CNS efficacy in NSCLC with BM in treatment-naïve (with/without radiotherapy) and -refractory patients suggests that alectinib will be a major new player in this indication.

1. Rangachari R, et al. Lung Cancer 2015;88:108–11
2. Mok T, et al. J Clin Oncol 2015;22(Suppl):8059
3. Sullivan I, Planchard D. Ther Adv Med Oncol 2016;8:32–47

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Efficacy for combined PD-1 inhibitor and cancer vaccine in HPV-16-positive cancer

A reduction in T-cell activity via tumour-mediated CTLA-4 and PD-1 signalling may contribute to the disappointing lack of success experienced with tumour vaccines in the clinic.¹ The introduction of checkpoint inhibitors as cancer treatments has led to a growing interest in cancer vaccines in combination with these new agents.

In a presentation yesterday, Professor Bonnie Glisson from MD Anderson Cancer Center, Houston, TX, USA, reported data from a phase II trial demonstrating the promising efficacy of a combination of nivolumab and the human papillomavirus (HPV)-16 vaccine, ISA 101, in 24 patients with recurrent, incurable HPV-16-positive cancer (Abstract 11360).

The trial met its primary endpoint, achieving an overall response rate (ORR) of 33%.



“The ORR of 36% in 22 patients with oropharyngeal cancer compares favourably with the 16% achieved with nivolumab monotherapy in similar patients in CheckMate 141,” said Professor Glisson. At a median follow-up of 8.6 months, the median overall survival had not been reached.

“These data suggest that anti-PD-1 therapy can enhance the effects of cancer vaccines by counteracting the immunosuppressive tumour microenvironment, and the findings should be confirmed in a larger, randomised trial,” observed Professor Glisson.

1. Ali OA, et al. Cancer Immunol Res 2016;4:95–100

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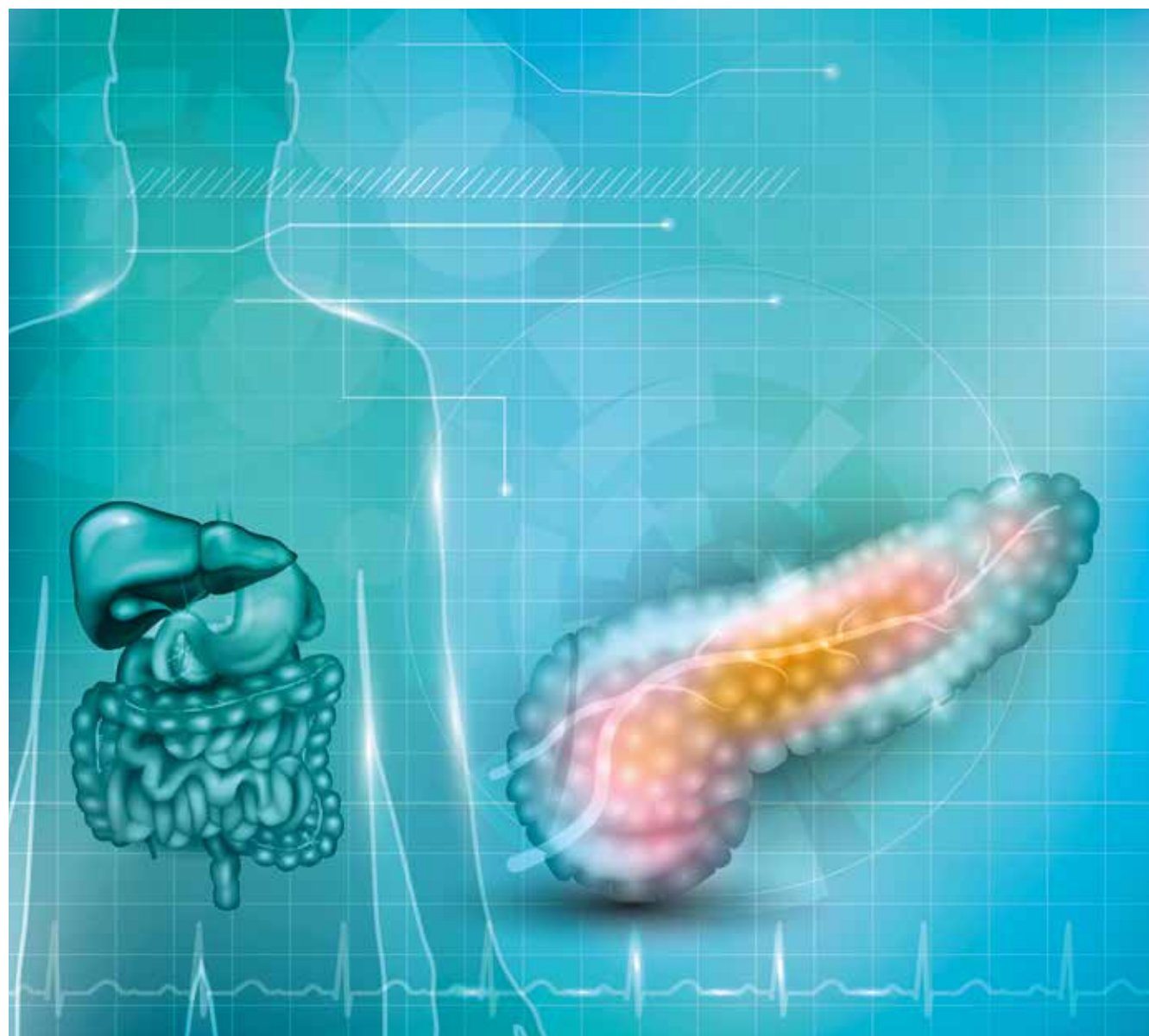
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Adjuvant treatment of biliary tract cancer comes of age in 2017

Updated results from the phase III PRODIGE-12–ACCORD 18 trial failed to show a significant improvement in survival with adjuvant gemcitabine plus oxaliplatin (GEMOX) over surveillance in patients with resected, localised biliary tract cancer, Dr Julien Edeline from Centre Eugene Marquis, Rennes, France, told delegates in a Late-Breaking Abstract presentation on Sunday (Abstract LBA29).

After a median of 46.5 months, median relapse-free survival (RFS) among the 196 patients was 30.4 months with GEMOX and 18.5 months with surveillance (hazard ratio [HR] 0.88; $p=0.47$). Median overall survival was 75.8 months with GEMOX and 50.8 months with surveillance (HR 1.08; $p=0.74$).

Further analyses did not reveal an RFS or OS benefit for GEMOX in any patient or risk sub-group. As anticipated, a higher incidence of grade 3–4 adverse events occurred with GEMOX (75%) than with surveillance (31%).

According to Professor Juan Valle from University of Manchester and The Christie NHS Foundation Trust, Manchester, UK there is a clear need to improve survival in patients undergoing potentially curative surgery for biliary tract cancer. Building on efficacy seen

in advanced disease, PRODIGE-12–ACCORD 18 evaluated the benefit of adjuvant GEMOX. Although adjuvant chemotherapy was numerically superior in terms of median RFS (the primary endpoint), relapse risk reduction was 12%, failing to reach statistical significance. These findings need to be viewed in the context of results from the BILCAP study ($n=447$),¹ which showed a survival benefit with capecitabine versus observation after radical surgery (HR 0.75; 95% confidence interval 0.58–0.97; median 36 to 53 months in the pre-specified per-protocol population). Based on these results, capecitabine has been adopted in many countries as the new standard of care in this setting. With a sample size of 196 patients, PRODIGE-12–ACCORD 18 had limited power to detect significant benefit and its results do not support the use of GEMOX as adjuvant treatment.

To date, the strongest evidence supports capecitabine as the adjuvant systemic therapy of choice.

Whether combination chemotherapy is better than capecitabine monotherapy is under evaluation in the ongoing ACTICCA-1 study.

1. Primrose JN, et al. J Clin Oncol 2017;35(Suppl):4006

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Three versus 6 months of adjuvant chemotherapy for CRC: Finally a definitive answer?



Angela Lamarca: Associate Editor of the ESMO 2017 Daily Reporter, The Christie NHS Foundation Trust, Manchester, UK

There has been much debate over the last decade about whether the standard 6 months of adjuvant oxaliplatin-based chemotherapy for colorectal cancer can be replaced by a shorter 3-month course. The main interest in such an approach is to minimise treatment-related toxicities—such as grade 3 sensory

neuropathy—which can be debilitating and long-lasting. In a Special Session yesterday, delegates heard updated results from the pivotal IDEA pooled analysis (Abstract LBA21_PR), together with the latest data from four of the six randomised phase III trials it included (Abstracts LBA22, LBA23, LBA24 and 4730).

IDEA enrolled 12,834 patients from 12 countries in trials between 2007 and 2015. Non-inferiority was defined as a disease-free survival hazard ratio (HR) upper level confidence interval (CI) <1.12. Sub-group analyses exploring impact by type of adjuvant chemotherapy (leucovorin, 5-fluorouracil, oxaliplatin [FOLFOX] versus capecitabine, oxaliplatin [CAPOX]) and risk group (T1–3/N1 versus T4/N2) were performed.



The IDEA results provide the basis for individual adjustments of adjuvant treatment duration based on risk of recurrence, patient preference, toxicity and chemotherapy regimen.

Non-inferiority could not be confirmed for the overall population (HR 1.07; 95% CI 1.00–1.15; Abstract LBA21_PR). Three months was non-inferior to 6 months for CAPOX (HR 0.95; 95% CI 0.85–1.06); in contrast, for patients treated with FOLFOX, inferiority was confirmed (HR 1.16; 95% CI 1.06–1.26; Abstract LBA21_PR). When analysed by risk group, 3 months was non-inferior to 6 months in low-risk disease (T1–3/N1)—but not in high-risk disease (T4/N2)—and was associated with significantly lower rates of neurotoxicity than 6-month treatment (Abstracts 4730, LBA24).

Professor Andrés Cervantes from the University of Valencia, Spain, said that while the IDEA project confirmed the reduced toxicity of the 3-month adjuvant oxaliplatin-based chemotherapy regimen compared with the 6-month regimen, the curative potential of the shorter regimen is not compromised in patients with T1–3/N1 disease. However, he added that, “For patients with high-risk disease features, 3-month adjuvant chemotherapy may have a reduced benefit.” Professor Cervantes said that the data generated by the IDEA project help to quantify risks and benefits, enabling discussion of the most appropriate approach according to individual disease characteristics and patient preferences.

Francesco De Lorenzo, President of the European Cancer Patient Coalition (ECPC) and a colon cancer survivor, recognised the important achievements of these trials. “Receiving a shorter treatment regimen while obtaining a non-inferior outcome means that these patients have a lower risk of treatment-related toxicities, as well as more freedom to return to a normal life. Furthermore, this approach also improves the sustainability of the healthcare system,” he observed.



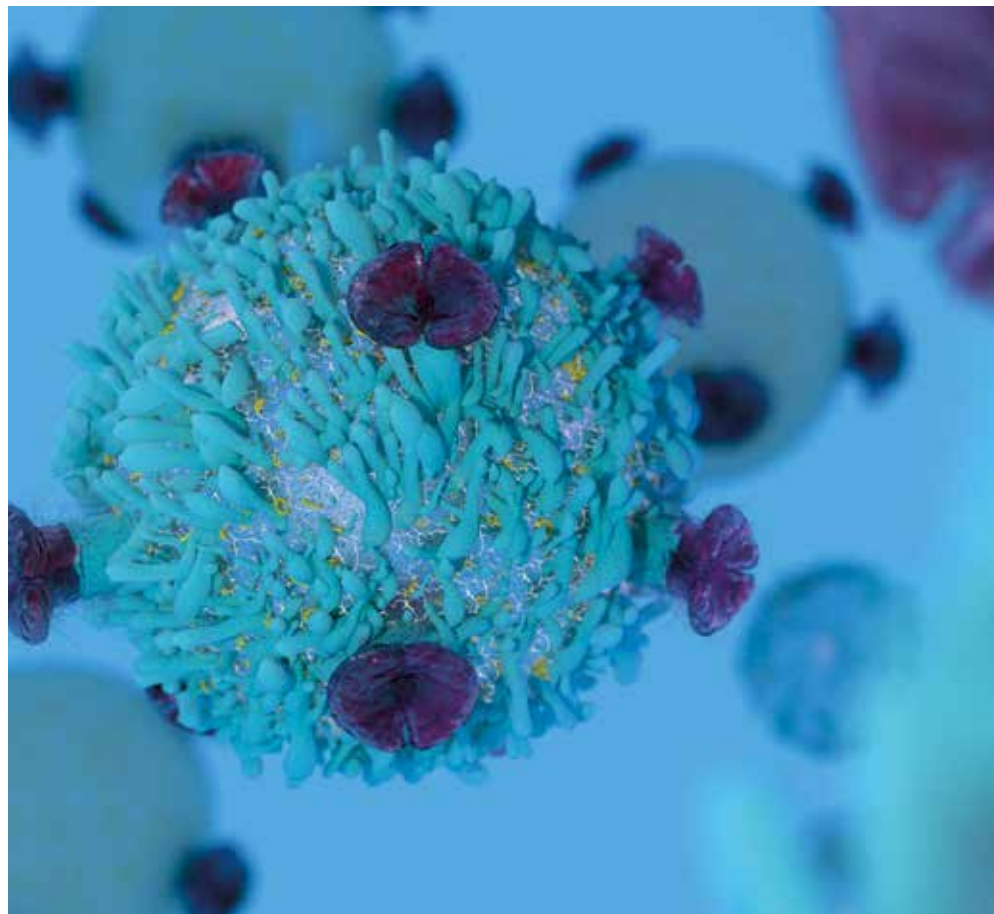
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Latest data on PD-1/PD-L1 inhibition beyond first-line in HNSCC



Immunotherapy has met with considerable enthusiasm in the treatment of recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) progressing on platinum-containing therapy.¹ PD-1 and PD-L1 can be expressed in immune cells infiltrating the tumour microenvironment and also on tumour cells,¹ although their impact on prognosis was unknown. A presentation on Saturday reported that median overall survival (OS) was 21.2 months longer in patients with HNSCC with $\geq 1\%$ versus low/no tumour cell PD-L1 expression (Abstract 1049PD), while no significant association was observed between immune cell PD-L1 expression and OS.

In 2016, the FDA granted approval in HNSCC for the anti-PD-1 agents pembrolizumab² and nivolumab,³ and a positive opinion for nivolumab was issued by the EMA in 2017.⁴

Yesterday, a Late-Breaking Abstract presentation reported that the phase III KEYNOTE-040 trial, conducted as a condition of the FDA's approval of pembrolizumab, failed to meet its primary endpoint; a 19% reduction in the risk of death compared with investigator's choice of therapy did not show

statistical significance as the pre-specified efficacy boundary was not reached (Abstract LBA45_PR).

In the same session, an analysis of the phase III CheckMate 141 study showed that nivolumab treatment beyond first progression may lead to tumour shrinkage in some patients, accompanied by changes in immune cell profiles similar to those observed in upfront responders (Abstract 10430).

Finally, earlier phase studies demonstrated the tolerability and antitumour efficacy of the anti-PD-L1 agents, durvalumab (Abstract 10420) and atezolizumab (Abstract 10440) after failure on previous treatment(s), with atezolizumab activity being observed even in patients with low/no PD-L1 expression.

1. Ran X, Yang K. Drug Des Devel Ther 2017;11:2007–14
2. www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm515627.htm
3. www.fda.gov/drugs/informationondrugs/approveddrugs/ucm528920.htm
4. www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion/human/003985/WC500224411.pdf

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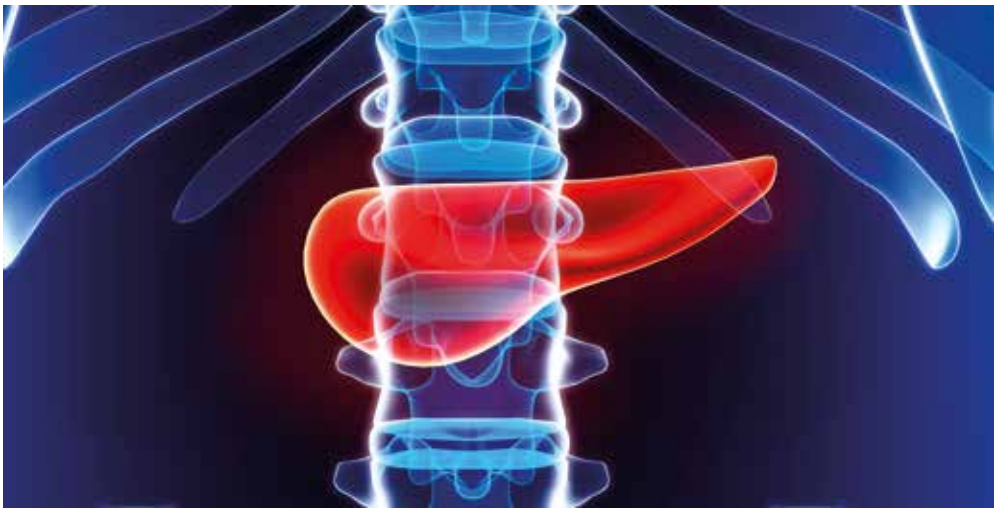
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Nab-paclitaxel plus gemcitabine shows promise in locally advanced pancreatic cancer



Locally advanced pancreatic cancer (LAPC) differs from metastatic pancreatic cancer in many aspects, such as natural behaviour and disease aggressiveness. Based on this rationale, patients diagnosed with LAPC have been excluded from clinical trials in which new chemotherapy combinations^{1,2} were being explored. Thus, access to new treatment alternatives for this patient population remains limited.

Following the success of its use in the treatment of metastatic pancreatic cancer,¹ combination chemotherapy with nab-paclitaxel plus gemcitabine was investigated in 101 patients with unresectable LAPC in the phase II LAPACT trial. Interim efficacy and safety results from the study were reported yesterday by Dr Philip Philip from Karmanos Cancer Institute, Detroit, MI, USA. After an induction period of six cycles of nab-paclitaxel plus gemcitabine,

patients received continuation chemotherapy, surgery or chemoradiotherapy, as per investigator's choice (Abstract 622PD).

Among 93 evaluable patients in the LAPACT study, the partial response and disease control rates were 35% and 82%, respectively. Following induction treatment, 14 patients (15%) underwent surgery.

Grade ≥ 3 adverse events included neutropenia (37%), anaemia (9%) and peripheral sensory neuropathy (4%).

Going one step further, another phase II study evaluated the nab-paclitaxel plus gemcitabine combination with/without the connective tissue growth factor inhibitor pamrevlumab in 33 treatment-naïve patients with LAPC. A potential improvement in resection rate from 17% to 44% was observed with the addition of the targeted agent (Abstract 1734PD).

Discussing the results, Dr Angela Lamarca from The Christie NHS Foundation Trust, Manchester, UK, and Associate Editor of the ESMO 2017 *Daily Reporter*, highlighted the importance of focusing ongoing and future research in this population of patients with LAPC, which has been poorly represented in previous studies. "Combination gemcitabine and nab-paclitaxel in LAPC has a similar toxicity profile to that in patients with metastatic disease. In addition, the proportion of patients whose cancer is converted into resectable disease warrants further investigation." She added, "Should these encouraging results be confirmed in larger randomised studies, this could represent a significant step forward for patients with LAPC."

1. Von Hoff DD, et al. N Engl J Med 2013;369:1691–703
2. Conroy T, et al. N Engl J Med 2011;364:1817–25

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METASTATIC BREAST CANCER
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At Pfizer Oncology, we know that women with metastatic breast cancer (mBC) know their own needs best. That's why we work side-by-side collaboratively with patients to co-create resources and services that truly meet the unique needs of women with mBC.

To drive change, we joined forces with the "Every day is precious" initiative, an international and multi-disciplinary group of mBC patients, BC survivors and patient advocates.

Explore our resources created by patients, for patients

Patients often have a whirlwind of questions and feelings following their diagnosis, not all of which can be addressed during doctor-patient conversations. Developed by the "Every day is precious" initiative, the **Me & mBC** information resource is intended to help patients understand and manage their disease, to get the most out of conversations with their doctors. The information is available in printed handbooks and online in English, with further language versions in development. **Please visit www.meandmbc.com**

Moreover, isolation has been identified as a key issue for women with mBC! The unique App **EmotionSpace** offers women living with mBC a secure space to record their feelings and optionally let family and friends know when they need extra support. The App is being launched in a number of countries across Europe. **Please visit your local App- or Play Store to check the availability in your country.**

1. Global Status of Advanced/Metastatic Breast Cancer: 2005 - 2015 Decade Report. Sponsored by Pfizer Oncology. March 2016. Available at: www.breastcancervision.com Accessed June 2017. PP-IBR-EUR-0488. Date of preparation: June 2017

Reportage – Day four



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