

INTEGRATING SCIENCE INTO ONCOLOGY FOR A BETTER PATIENT OUTCOME

# DAILY REPORTER

MONDAY 11 SEPTEMBER 2017

## Neoadjuvant chemotherapy plus surgery is not superior to standard chemoradiotherapy for locally advanced cervical cancer



For locally advanced cervical cancer, neoadjuvant chemotherapy followed by surgery (NACT–surgery) may offer outcome benefits versus surgery or radiotherapy alone,<sup>1</sup> but until now there has been no formal comparison with the standard approach of cisplatin-based chemoradiotherapy (CRT).

In yesterday's Presidential Symposium II, Professor Sudeep Gupta from Tata Memorial Centre, Mumbai, India, reported results from a randomised trial in 633 patients with stage IB2–IIB squamous cell carcinoma of the cervix demonstrating that NACT–surgery was not superior to CRT in this setting (Abstract 9280\_PR). CRT resulted in significantly higher 5-year disease-

free survival compared with NACT–surgery (primary endpoint; 76.7% versus 69.3% of patients; hazard ratio [HR] 1.38;  $p=0.038$ ). There was no significant difference in 5-year overall survival between the two treatment arms (74.7% versus 74.8%; HR 1.025;  $p=0.87$ ). Toxicity of both treatments was acceptable.

Commenting on these findings, Professor Nicoletta Colombo from Istituto Europeo di Oncologia, Milan, Italy, observed, "It took 12 years to complete this trial, which gave us important clinical information. Although NACT–surgery did not prove to be superior to CRT in terms of efficacy, a positive impact on quality of life, particularly in young patients, cannot be excluded. A recently completed European Organisation for Research and Treatment of Cancer trial addressing the same comparison will help to clarify this extremely relevant outcome."

1. Lapresa M, et al. Expert Rev Anticancer Ther 2015;15:1171–81



Nicoletta Colombo from Istituto Europeo di Oncologia, Milan, Italy



### Erratum



An article in Sunday's *Daily Reporter* (page 6) entitled 'Osimertinib: A new first-line option for *EGFR* T790M-positive NSCLC' should have been 'Osimertinib: a new first-line option for *EGFR* mutated NSCLC'. A corrected version of the article can be found online.

# Few FDA-approved palliative anticancer drugs meet ESMO-MCBS-defined benefit

Introduced in 2015 as a tool to quantify the clinically meaningful benefit of an anticancer drug,<sup>1</sup> the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) has shown utility for supporting treatment decisions in clinical practice<sup>2,3</sup> and assigning a score for newly approved drugs within ESMO's Clinical Practice Guidelines.<sup>4</sup>

A presentation in a Proffered Paper Session today will report that over one-quarter of the anticancer drugs approved for palliative use by the US FDA over the last decade achieved a clinically meaningful benefit according to the ESMO-MCBS (Abstract 14350\_PR). Ms Consolación Molto Valiente from Hospital de la Santa Creu i Sant Pau and Universitat Autònoma de Barcelona, Spain, will explain that of the 63 individual anticancer drugs approved for 118 indications between January 2006 and December 2016, 46% received orphan drug designation. The

ESMO-MCBS threshold for clinical benefit was achieved by 29% of orphan drugs and 27% of non-orphan drugs approved for palliative use. Orphan drug designation does not appear to influence the odds of meeting the ESMO-MCBS clinically meaningful benefit threshold.

**Find out more about ESMO-MCBS applications in today's 'Public health policy and health economics' session (16.30 – 18.00, Alicante).**

1. Cherny NI, et al. Ann Oncol 2015;26:1547–73
2. Kiesewetter B, et al. ESMO Open 2016;1:e000066
3. Kiesewetter B, et al. ESMO Open 2017;2:e000166
4. [www.esmo.org/Press-Office/Press-Releases/Launch-of-First-eUpdate-Integrating-Breakthroughs-in-ESMO-Clinical-Practice-Guidelines](http://www.esmo.org/Press-Office/Press-Releases/Launch-of-First-eUpdate-Integrating-Breakthroughs-in-ESMO-Clinical-Practice-Guidelines)

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# Further clarification on the place of abiraterone in high-risk prostate cancer



**Johann de Bono:** Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, UK

**A Proffered Paper Session on Friday included a number of ground-breaking new findings for patients with locally advanced or metastatic high-risk prostate cancer. Current ESMO clinical practice guidelines<sup>1</sup> recommend neoadjuvant and concurrent androgen deprivation therapy (ADT) for men with localised or locally advanced high-risk disease receiving radical radiotherapy (RT). For men with castration-sensitive advanced prostate cancer, the recommendation is ADT alone or, in selected patients, ADT with docetaxel.**

Following the finding of a survival advantage with the androgen synthesis inhibitor abiraterone in men with castrate-resistant prostate cancer,<sup>2</sup> this agent was investigated earlier in the disease course in men with high-risk and hormone-sensitive prostate cancer. Improved survival outcomes were shown with either abiraterone or docetaxel added to ADT with/without RT in hormone-sensitive prostate cancer in the STAMPEDE study.<sup>3,4</sup> In order to help guide clinicians' treatment decisions, abiraterone and docetaxel data from STAMPEDE (n=566 patients) were compared at a median follow-up of 4 years. Dr Matt Sydes (University College London, UK; Abstract LBA31\_PR) reported no statistically significant difference between docetaxel and abiraterone arms in terms of overall survival (hazard ratio [HR] 1.16; 95% confidence interval (CI) 0.82–1.65). However, abiraterone was clearly superior in terms of failure-free (FFS; HR 0.51; 95% CI 0.39–0.67) and progression-free survival (PFS; HR 0.65; 95% CI 0.48–0.88), and had marginal superiority in terms of metastatic-free survival (MFS; HR 0.77; 95% CI 0.57–1.03) and symptomatic skeletal events (HR 0.83;

95% CI 0.55–1.25). Dr Sydes advised that drug availability was likely to drive treatment choice.

Professor Nicholas James (Queen Elizabeth-University Hospital Birmingham NHS Foundation Trust, UK; Abstract LBA34) provided additional support for abiraterone plus ADT with/without RT in this setting, reporting that in a sub-group analysis of patients in the non-metastatic high-risk prostate cancer cohort of STAMPEDE. At a median follow-up of 38 months, FFS was improved in patients with NOMO disease by the addition of abiraterone (HR 0.14; 95% CI 0.07–0.30) with 3-year FFS of 98% versus 82% in patients who did not receive abiraterone. Abiraterone also improved FFS among patients with N+M0 disease (HR 0.26; 95% CI 0.17–0.40). Professor James said that MFS improvements in both NOMO and N+M0 sub-groups also suggest a likely translation into a survival advantage with the addition of abiraterone.

Finally, Dr Kim Chi (BC Cancer Agency, Vancouver, British Columbia, Canada; Abstract 7830) presented the first data of patient-reported outcomes from the LATITUDE

study in men with high-risk metastatic, hormone-sensitive prostate cancer, showing that abiraterone and prednisone plus ADT significantly delayed the progression of pain and fatigue intensity and functional decline.

The findings have the potential to bring about a paradigm shift in the treatment of high-risk prostate cancer. Now, we are witnessing upfront full androgen blockade with the combination of ADT and abiraterone, and it would be interesting to know how this compares with luteinizing hormone-releasing hormone agonists, with or without docetaxel. The hope is for more personalised therapy, with a clear indication of which patients should receive chemotherapy and which should receive abiraterone with their ADT.

1. Parker C, et al. Ann Oncol 2015;26 (Suppl 5):v69–77
2. Ryan CJ, et al. Lancet Oncol 2015;16:152–60
3. James ND, et al. N Engl J Med 2017;377:338–51
4. James ND, et al. J Clin Oncol 2017;35(Suppl):Abstract LBA5003



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Your choice of career path in oncology (pre-registration required).  
09.30 – 10.30, Rooms 1 & 2

### Brunch

Critically ill cancer patients: Patient selection for admission to ICU  
11.00 – 11.45, Salamanca

### Special Session

Fellowships in Europe: Educational opportunities for young oncologists  
14.15 – 15.45, Salamanca

Find out more here!



# Pan-TRK inhibitor enters phase II clinical testing for paediatric patients



**Neurotrophic tropomyosin receptor kinase (NTRK) genes encode a family of TRK receptors that play a critical role in the regulation of growth, differentiation and survival of neurons through activation by neurotrophins. Abnormalities within these genes have been identified in a range of tumour types, including paediatric malignancies, and have recently emerged as novel targets for cancer therapy.<sup>1</sup>**

A growing number of TRK inhibitors are now in clinical development,<sup>1</sup> including LOXO-101

or larotrectinib, the first selective small-molecule pan-TRK inhibitor to enter clinical trials. Impressive clinical activity was previously demonstrated with larotrectinib across multiple tumour types in patients with *NTRK*-translocated cancers.<sup>2</sup>

A phase I/II international trial of paediatric patients ( $\geq 1$  month of age) with *NTRK*-translocated tumours, including infantile fibrosarcoma and primary CNS tumours, has recently been initiated (SCOUT; NCT02637687). The recommended

phase II dose has been established for paediatric use (100 mg/m<sup>2</sup>) and enrolment to phase II began in April 2017, with objective response rate as the primary endpoint (Abstract 418TiP).

**Details of the clinical trial of larotrectinib in paediatric patients will be presented during today's Poster Display Session 'Developmental therapeutics' (13.15 – 14.15, Hall 8).**

Professor Ulrik Lassen from Copenhagen University Hospital Rigshospitalet, Denmark, commented, "Striking results have been achieved with larotrectinib in adult cancers, with durable response rates of close to 80%. The *NTRK* translocation may be more frequent in paediatric cancers and I believe that larotrectinib may be the next tumour agnostic agent to be approved."

1. Amatu A, et al. ESMO Open 2016;1:e000023
2. Hyman DM, et al. J Clin Oncol 2017;35(Suppl):LBA2501



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# Optimising treatment with CDK4 inhibitors in metastatic breast cancer



**Giuseppe Curigliano:** Editor-in-Chief of the ESMO 2017 Daily Reporter; European Institute of Oncology, Milan, Italy

**Resistance to endocrine therapies is inevitable in advanced hormone receptor (HR)-positive breast cancer.<sup>1</sup> Cyclin-dependent kinase (CDK) 4/6 inhibitors may overcome endocrine resistance, and two agents (palbociclib and ribociclib) are approved as first-line treatment for HR-positive, HER2-negative advanced or metastatic breast cancer in combination with an aromatase inhibitor. Phase III**

**data on abemaciclib, a third agent in this indication, were presented yesterday (MONARCH 3; Abstract 2360\_PR). On a background of anastrozole or letrozole, abemaciclib significantly prolonged progression-free survival (PFS) versus placebo (not reached versus 14.7 months, respectively; hazard ratio 0.543; 95% confidence interval 0.409–0.723; p=0.00021) in patients with metastases without prior systemic treatment (n=493). Objective response rates were 59.2% and 43.8% in the abemaciclib and placebo arms, respectively (p=0.004). The most frequent adverse events were diarrhoea and neutropenia.**

In exploratory sub-group analyses, addition of abemaciclib in patients with liver metastases conferred substantial benefit (12-month PFS achieved by 61.5% and 31.4% of patients given abemaciclib or placebo, respectively), while among those with bone-only disease, rates of 12-month PFS were high in both treatment arms (86.0% and 75.7% of patients, respectively). These findings suggest that single-agent endocrine therapy may be an appropriate initial treatment for patients with a good prognosis.

Further work is needed to make the best use of CDK4/6 inhibitors in clinical practice. Professor Nicholas Turner of The Royal Marsden NHS Foundation Trust, London, UK, principal investigator of the palbociclib PALOMA-3 trial,<sup>2</sup> commented, "Optimising the use of these agents will require predictive biomarkers to guide appropriate patient selection (potentially including subsets with triple-negative disease) and trials to establish the most appropriate order in which to administer single agents and/or specific combinations."



**Latest data with CDK4 inhibitors, including triple combinations with PI3K inhibitors, from Saturday's Educational Session ('CDK4 inhibitors in metastatic breast cancer') are now available via webcast.**

1. Turner NC, et al. Lancet 2017;389:2403–14
2. Turner NC, et al. N Engl J Med 2015;373:209–19



# Checkpoint inhibitors are active as second- or third-line therapy for mesothelioma

There are no standard treatment options for malignant pleural mesothelioma (MPM) failing first-line platinum–folate antimetabolite therapy<sup>1</sup> and the use of checkpoint inhibitors in this setting has led to mixed results.<sup>2</sup> Yesterday, a Late-Breaking Abstract presentation by Professor Gérard Zalcman from Université Paris-Diderot, Paris, France, suggested that the anti-PD-1 antibody nivolumab, alone or in combination with the anti-CTLA-4 antibody ipilimumab, may provide meaningful clinical efficacy (Abstract LBA58\_PR).

In a non-comparative, randomised, phase II trial in 125 patients with MPM relapsing after 1–2 prior lines of therapy, the 12-week disease control rate (primary endpoint) was 44.4% for nivolumab and 50.0% for nivolumab–ipilimumab. At a median follow-up of 15 months, the median progression-free survival times were 4.0 months for nivolumab and 5.6 months for nivolumab–ipilimumab.

**The median overall survival of 13.6 months for nivolumab and not reached for nivolumab–ipilimumab compare favourably with those for first-line chemotherapy<sup>2</sup> in patients with MPM.**

Professor Zalcman concluded that these findings support a recent National Comprehensive Cancer Network (NCCN) decision to recommend nivolumab monotherapy or combination therapy as second- or third-line options in relapsing MPM.

- 1. Baas P, et al. Ann Oncol 2015;26(Suppl 5):v31–9
- 2. Ceresoli GL, et al. Expert Rev Anticancer Ther 2016;16:673–5

# Dual blockade in breast cancer: Different receptors, different outcomes

Dual HER2 blockade using agents with complementary mechanisms of action improves outcomes compared with monotherapy in patients with untreated HER2-positive metastatic breast cancer (mBC).<sup>1</sup> HER2 is involved in cardiac homeostasis and stress response, however the risk of cardiotoxicity with dual HER2 blockade does not appear to be increased compared with single anti-HER2 agents. Strain rate imaging of 27 women with mBC given trastuzumab plus pertuzumab and docetaxel detected subtle changes in longitudinal and radial left ventricular function after eight cycles of therapy (Abstract 296P). This methodology could be used for the early detection of preclinical myocardial dysfunction in patients undergoing dual HER2 blockade, but further studies are needed using this in daily practice.

Dual hormone receptor (HR) blockade using the aromatase inhibitor anastrozole and the selective oestrogen receptor degrader fulvestrant showed promising efficacy in preclinical models.<sup>2</sup> But, the FACT study of first-line anastrozole plus fulvestrant in women with HR-positive early BC failed to show increased survival or time to progression versus anastrozole alone.<sup>2</sup> In light of these results, a 6-year follow-up study of the same combination in HR-positive patients with early BC lost funding and failed to recruit sufficient patients (Abstract 1480). Anastrozole plus fulvestrant was not associated with an increased 5-year disease-free survival rate, although the underpowered study and insufficient fulvestrant dose administered (81% median relative dose intensity) precluded formal conclusions being made. Current evidence, however, does not support pursuing dual HR blockade in early BC.

- 1. Gianni L, et al. Lancet Oncol 2012;13:25–32
- 2. Bergh J, et al. J Clin Oncol 2012;30:1919–25

# Selective internal radiation therapy shows promise in liver disease

Patients with intra-hepatic cholangiocarcinoma (ICC) and hepatocellular carcinoma (HCC) often present with relatively advanced disease when therapeutic options are limited and prognosis is poor.<sup>1</sup> Consequently, loco-regional therapies that may downstage a malignancy and enable surgical resection or liver transplantation represent an attractive strategy. One such treatment, selective internal radiation therapy (SIRT) with yttrium-90 spheres, was included in the 2016 ESMO Clinical Practice Guidelines for chemotherapy-refractory/intolerant colorectal liver metastases and was the subject of two presentations on Saturday.

Dr Julien Edeline from Centre Eugene Marquis, Rennes, France (Abstract 711P) reported promising activity in 41 patients with advanced ICC who received SIRT plus chemotherapy in a prospective, single-arm phase II study. The response rate according to RECIST (primary endpoint) was 39% and disease control was experienced by all 40 evaluable patients. Notably, nine patients (22%) were down-staged to surgery and of these, eight (20%) achieved R0 resection. Median overall survival (OS) was 21 months.

**SIRT plus chemotherapy resulted in down-staging of ICC in 22% of patients.**

Dr Ahmed Kaseb from University of Texas MD Anderson Cancer Center, Houston, TX, USA (Abstract 709P) shared data from the first prospective (phase II) study to evaluate SIRT plus sorafenib in 38 patients with advanced HCC. Longer median OS (18.5 months) was reported for the combination compared with previous reports for sorafenib alone (10.7 months<sup>2</sup>) in patients with advanced HCC.

The combination of SIRT plus chemotherapy and SIRT plus sorafenib had manageable toxicity and should be further evaluated in this patient population.

- 1. Wang EA, et al. J Gastrointest Oncol 2017;8:266–78
- 2. Llovet JM, et al. N Engl J Med 2008;359:378–90

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# Continued advances in the treatment of genitourinary cancers



**Cora N. Sternberg:** San Camillo-Forlanini Hospital, Rome, Italy

Use of immunotherapies in the treatment of bladder and urothelial cancers is, again, a major theme at ESMO 2017, while other new agents, combinations, and predictive markers are also coming to the fore.

Late-Breaking Abstracts regarding advanced or metastatic urothelial cancer (mUC) were reported, including mature efficacy and safety data from the

KEYNOTE-045 study demonstrating superiority of pembrolizumab over chemotherapy as second-line treatment (Abstract LBA37\_PR). Sub-group analysis from KEYNOTE-045 revealed that pembrolizumab was associated with better outcomes than single-agent docetaxel, paclitaxel or vinflunine, with less frequent adverse events (Abstract 851PD).

A reduction in tumour burden post-progression and improved overall survival were reported for selected patients who continued versus discontinued atezolizumab in IMVIGOR210 (Abstract 852PD), while tumour infiltrating lymphocytes and an epithelial-mesenchymal transition gene expression signature both show potential as predictive markers of nivolumab response (Abstracts 848PD and 850PD).

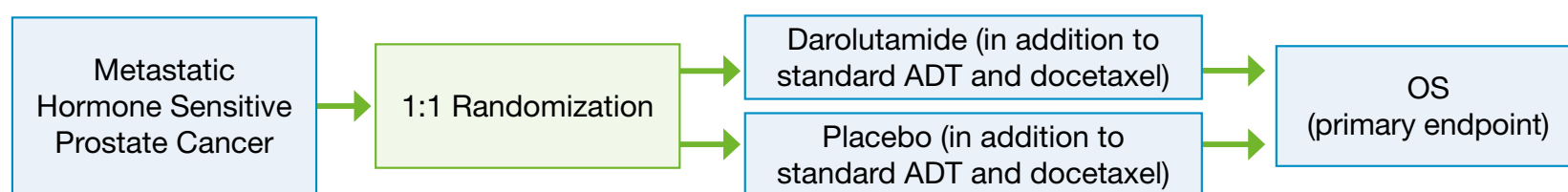
Positive results were also reported from the phase III RANGE trial—in which a proportion of patients had received prior immune checkpoint inhibitor therapy—showing a statistically significant increase in progression-free survival (PFS) with the addition of ramucirumab to docetaxel in patients with platinum-refractory disease (Abstract LBA4\_PR).

Phase I data on cabozantinib in combination with nivolumab with or without ipilimumab in mUC (Abstract 8460) and phase Ib/II data on lenvatinib in combination with pembrolizumab in renal cell carcinoma (RCC) show promising antitumour activity and manageable toxicity (Abstract 8470). Another study on the most effective sequence of two multikinase inhibitors in metastatic RCC (mRCC) could not demonstrate that pazopanib followed by sorafenib at disease progression resulted in longer total PFS compared with the reverse sequence of the agents (Abstract 8450). Results of the most effective timing of administration of the multikinase inhibitor sunitinib in mRCC—either pre-surgically followed by cytoreductive nephrectomy (CN) in the absence of disease progression or after immediate CN—showed that the progression-free rate at 28 weeks (the primary endpoint) was unaffected by the sequence, although an overall survival improvement was observed for upfront sunitinib before CN (hazard ratio 0.57;  $p=0.032$ ) (Abstract LBA35).

Major advances have taken place with the advent of checkpoint inhibitors for patients with advanced UC. Although better than single-agent chemotherapy, unfortunately only a fraction of patients will achieve long-term survival. Combination therapy and better patient selection through predictive markers offer promise. A novel combination with the addition of ramucirumab to docetaxel in patients with platinum-refractory disease offers another therapeutic option with a different mechanism of action to immunotherapy.

For RCC there has been major progress in the last decade with the approval of tyrosine kinase inhibitors (TKIs) and nivolumab immunotherapy. Predictive markers of response are being developed and are desperately needed. There are several ongoing phase III trials of immunotherapy combinations and of immunotherapy and TKIs, including the CheckMate 214 study of nivolumab and ipilimumab versus sunitinib as first-line therapy for advanced RCC presented yesterday, which showed improved overall survival in patients with intermediate and poor-risk RCC (Abstract LBA5).

## NOW ENROLLING: Efficacy and Safety Study of Darolutamide (ODM-201) in Men with Metastatic Hormone Sensitive Prostate Cancer (ARASENS)



### Primary Objective

- Overall Survival

### Secondary Objectives

- Time to castration resistant prostate cancer
- Time to initiation of subsequent antineoplastic therapy
- Symptomatic skeletal event free survival (SSE-FS)
- Time to first symptomatic skeletal event (SSE)
- Time to initiation of opioid use
- Time to pain progression
- Time to worsening of physical symptoms of disease
- Number of participants with adverse events as a measure of safety and tolerability

### Selected Inclusion Criteria:

- Histologically or cytologically confirmed adenocarcinoma of prostate.
- Metastatic disease
- Candidates for ADT and docetaxel. Started ADT with or without first generation anti androgen, but no longer than 12 weeks before randomization

- An Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate bone marrow, liver and renal function

### Selected Exclusion Criteria:

- Prior treatment with: LHRH agonist/antagonists; second generation androgen receptor (AR) inhibitors such as enzalutamide, ARN-509, Darolutamide (ODM-201); other investigational AR inhibitors; CYP17 enzyme inhibitor such as abiraterone acetate or oral ketoconazole as antineoplastic treatment for prostate cancer, chemotherapy, or immunotherapy for prostate cancer prior to randomization.
- Treatment with radiotherapy within two weeks before randomization
- Gastrointestinal disorder or procedure that is expected to interfere significantly with absorption of study treatment.
- Inability to swallow oral medications

**Darolutamide (ODM-201) is an investigational agent and is not approved by the FDA, EMA, or other health authorities.**

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For complete information please visit:  
<http://www.clinicaltrials.gov> (NCT02799602)

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# Antibody–drug conjugates: A potent option for hard-to-treat cancers



Rodrigo Dienstmann: Associate Editor of the ESMO 2017 Daily Reporter; Vall d'Hebron Institute of Oncology, Barcelona, Spain

Antibody–drug conjugates (ADCs) use tumour-specific antibodies to target highly potent cytotoxic agents directly to cancer cells; however, treatment-limiting adverse events may occur before the optimal therapeutic dose is achieved.<sup>1</sup> This profile of potency and risk has directed ADC development toward chemotherapy-refractory malignancies, such as triple-negative breast (TNBC), urothelial (UC), small-cell lung (SCLC) and colorectal cancers. The ADCs trastuzumab emtansine, brentuximab vedotin and inotuzumab ozogamicin have been EMA approved for

HER2-positive breast cancer, CD30-positive Hodgkin's lymphoma and CD22-positive acute lymphoblastic leukaemia, respectively. There is increased interest in ADC drug development, with ~100 ongoing clinical trials evaluating >80 ADCs against 59 unique targets (Abstract 1669P).

Trop-2-targeted sacituzumab govitecan has demonstrated promising efficacy in phase II studies of heavily pre-treated metastatic SCLC<sup>2</sup> (objective response rate [ORR], 14%), TNBC (ORR, 21%),<sup>3</sup> and, as presented yesterday, in 41 patients with pre-treated metastatic UC (ORR, 34%) (Abstract 858P). In the latter interim analysis, an impressive median response duration of 12.9 months and a median progression-free survival of 7.2 months was reported in a chemotherapy- and immunotherapy-refractory setting. Neutropenia (grade ≥3) occurred in 28% of patients. ADCs may be a valuable alternative for patients with hard-to-treat cancers and few treatment options.

1. de Goeij BE, Lambert JM. Curr Opin Immunol 2016;40:14–23  
2. Gray JE, et al. Clin Cancer Res 2017. Jul 5. Epub ahead of print  
3. Bardia A, et al. J Clin Oncol 2015;33(Suppl):1016



## Frances Shepherd receives the ESMO Women for Oncology Award

Frances Shepherd of the University of Toronto and Princess Margaret Hospital Cancer Centre, Toronto, Canada, was presented with the ESMO Women for Oncology Award by Fortunato Ciardiello in Saturday's Women for Oncology Session.

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# Less is more and more is more

It is currently unclear whether patients with high-risk endometrial cancer (EC) benefit from adjuvant chemotherapy given during and after radiotherapy (CTRT). A large, randomised intergroup trial (PORTEC-3) that compared CTRT with pelvic radiotherapy (RT) in women with high-risk EC suggests that this may not be the case for all patients. Five-year failure-free survival (FFS) did not significantly differ between the treatment arms (75.5% versus 68.9% in CTRT and RT arms, respectively; hazard ratio [HR] 0.77). Patients with stage III EC derived greatest benefit from CTRT; 5-year FFS was 69.3% for CTRT versus 58.0% for RT (p=0.032).

Learn more about the relative benefits and indications for surgery, chemotherapy and radiotherapy in EC in today's case-based Multidisciplinary Session ('Management of high risk early stage endometrial cancer'; 11.00 – 12.00, Granada).

Questions also remain about the role of secondary cytoreductive surgery in the platinum-sensitive recurrent ovarian cancer (PSROC) setting. An interim analysis from a phase III, randomised (ENGOT) trial in patients with PSROC and positive AGO score at first relapse suggests that surgery is beneficial; compared with chemotherapy alone, surgery followed by chemotherapy significantly increased progression-free survival (19.6 months versus 14 months; HR 0.66; 95% CI 0.52–0.83; p<0.001) and time to start of first subsequent therapy (21 months versus 13.9 months; HR 0.61; 95% CI 0.48–0.77; p<0.001). Final overall survival data are awaited.



Keep up to date with the latest evidence:  
Take a look at the webcast from  
Saturday's Educational Session,  
'How to manage ovarian cancer in 2017.'



Public health and health policy sessions not to be missed today!

**Patient Advocacy Track**


The Hans Keulen Memorial Debate:  
Lost in rehabilitation  
13.00 – 14.30, Cartagena

**Educational Session**

The 'micro-economics' of cancer: How the medical oncologist should micro-manage limited resources 14.45 – 16.15, Alicante



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# Which toxicities matter?



**Markus Joerger:** Associate Editor of the ESMO 2017 Daily Reporter; Cantonal Hospital, St. Gallen, Switzerland

The Common Terminology Criteria for Adverse Events, originally developed for reporting the scope and severity of adverse events (AEs) in clinical trials, are also increasingly used to guide treatment decisions in routine care.<sup>1</sup> Because most patients experience a range of mild-to-

moderate (grade I–II) AEs with anticancer treatment there is a risk that we, as clinicians, can overlook these events while focusing on the severe or life-threatening grade III–IV AEs most often used to characterise the safety profiles of new anticancer drugs. However, for our patients, chronic, lower grade AEs often have a hugely negative impact on quality of life, and this is a particularly important consideration within the supportive care setting.

To hear more about the toxicities that matter to our patients, don't miss the Special Symposium today 'Are grade III/IV toxicities the only ones that matter?' (09.15 – 10.45, Cordoba).

**Chronic, lower grade AEs often have a hugely negative impact on quality of life.**

1. Zhang S, et al. BMC Cancer 2016;16:392

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## Can immunotherapy cure advanced cancer?

The promise of cancer immunotherapy has been widely publicised in the media over recent years. Headlines suggesting 'lasting cure prospects' have offered hope to many patients with different tumour types. But do the clinical trial data live up to these exciting claims? Novel immunotherapies that harness the body's own immune system to induce an anticancer attack have certainly been associated with impressive responses, particularly in patients with melanoma where long-term remissions have been documented.<sup>1</sup> A significantly increased median time to distant metastasis has also been demonstrated with immune checkpoint inhibitors in some patients with locally advanced non-small-cell lung cancer, as highlighted in a Late-Breaking durvalumab abstract during Saturday's Presidential Symposium (Abstract LBA1\_PR).

However, can this prolonged time to relapse ultimately translate into cure? Professor John Haanen (Netherlands Cancer Institute, Amsterdam) will share his views on this important topic in a Keynote Lecture today, 'Does immunotherapy cure advanced cancer?' (08.15 – 09.00, Barcelona).

**Novel immunotherapies that harness the body's own immune system have been associated with impressive responses.**

1. Redman JM, et al. BMC Medicine 2016;14:20

## A new first-line standard of care for patients with advanced RCC

At the Presidential Symposium II yesterday, positive new survival data were presented from a phase III study (CheckMate 214) of nivolumab and ipilimumab versus sunitinib in 1,096 treatment-naïve patients with advanced renal cell carcinoma (RCC; Abstract LBA5). Dr Bernard Escudier from Institut Gustave Roussy, Villejuif, France noted that in patients with intermediate/poor risk disease (n=847), a highly statistically significant survival advantage was reported with the immunotherapy combination compared with sunitinib—a current standard of care anti-angiogenic tyrosine kinase inhibitor (TKI) in this setting—median overall survival: not reached (NR) versus 26.0 months, respectively; hazard ratio 0.63; 99.8% confidence interval 0.44–0.89; p<0.0001. A significantly higher objective response rate (42% versus 27%, respectively; p<0.0001) and longer median duration of response (NR versus 18.2 months) was also demonstrated

with nivolumab and ipilimumab compared with sunitinib in this patient sub-group. Particular benefit was observed in tumours with high (≥1%) PD-L1 expression.

**The immune checkpoint inhibitor combination was associated with a 37% reduction in the risk of death compared with sunitinib—a current standard of care anti-angiogenic TKI in this setting.**

Dr Escudier added that the immunotherapy arm was associated with a lower incidence of treatment-related adverse events (including high-grade events) and with better symptom control compared with the sunitinib arm.

Concluding, he suggested that these results support the use of the nivolumab and ipilimumab combination as a new first-line standard of care option for patients with advanced RCC.

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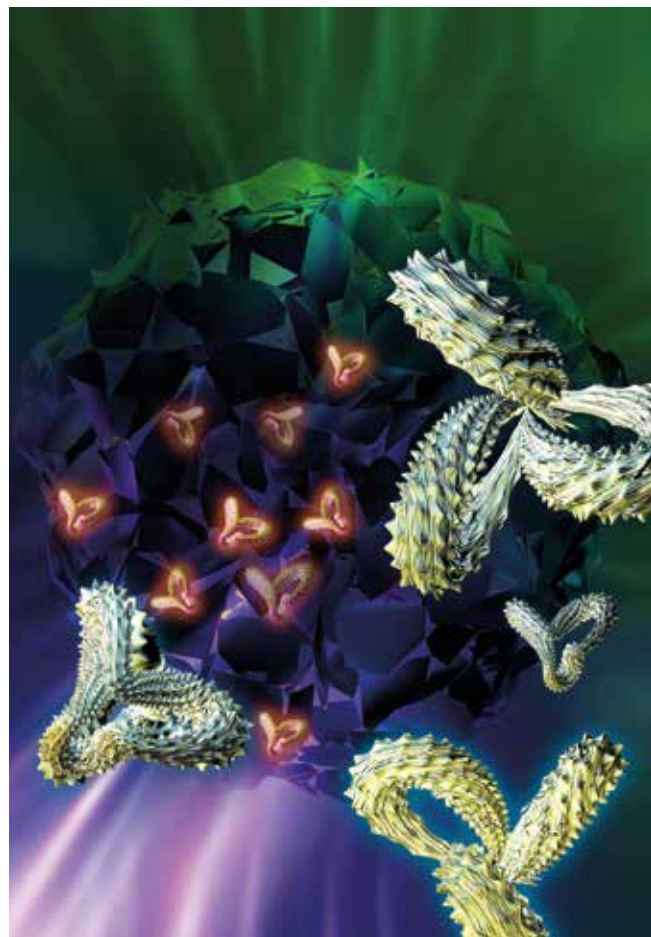


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# New combination shows promise in anti-PD-L1/PD-1-resistant melanoma



Heavily pre-treated patients with melanoma whose disease has progressed despite anti-PD-L1/PD-1 therapy may benefit from a new combination of nivolumab and the anti-lymphocyte activation gene-3 (LAG-3) monoclonal antibody (relatlimab), according to data presented in a Late-Breaking Abstract yesterday by Dr Paolo Ascierto from the Istituto Nazionale Tumori Fondazione G Pascale, Naples, Italy (Abstract LBA18). Dr Ascierto described updated findings (in all-comer and biomarker-enriched populations) from a previously presented phase I/IIa study<sup>1</sup> of patients progressing on prior anti-PD-L1/PD-1 treatment for melanoma.

In 61 patients evaluable for response, the objective response rate (ORR) was 11.5%, the disease control rate was 49% and the median duration of response was not reached. Also, 34% of patients had not experienced disease progression at the time of data analysis. Dr Ascierto pointed out that responses were more likely to occur in patients with LAG-3 expression  $\geq 1\%$  (ORR 18%); PD-L1 expression did not appear to enrich for response.

Among patients with LAG-3 expression  $\geq 1\%$ , ORR was higher among those with no *BRAF* mutation and those who received prior anti-CTLA-4 treatment.

The combination was well tolerated, with a safety profile similar to that of nivolumab monotherapy; among the 270 patients treated in the dose-escalation and -expansion phases, grade 3–4 treatment-related adverse events (TRAEs) occurred in 10%, with grade 3–4 TRAE-related discontinuations in 3%.

In response to these findings, Professor Reinhard Dummer from University Hospital Zurich, Switzerland, said, “These data are encouraging. Firstly, there is a chance to rescue patients failing anti-PD-1 therapy with another well-tolerated immunotherapy combination. Secondly—and even more relevant—LAG-3 expression will guide us to select patients. We urgently need to investigate whether LAG-3 expression analysis alone or in combination with PD-L1 staining constitute biomarkers for precision immunotherapy.”

**Encouraging activity is suggested with a novel anti-LAG-3 plus nivolumab combination in heavily pre-treated, anti-PD-L1/PD-1-resistant melanoma.**

1. Ascierto P, et al. J Clin Oncol 2017;35(Suppl):9520



**ESMO  
YOUNG  
ONCOLOGISTS**

## Networking to make a difference together

Over 200 enthusiastic participants gathered for the Young Oncologists Networking Evening on Saturday to make new contacts and share experiences with peers from around the world. Jointly hosted by ESMO's Young Oncologists Committee, the European Association for Cancer Research (EACR), the Sociedad Española de Oncología Médica (SEOM) and the Asociación Española de Investigación

sobre el Cáncer (ASEICA), the event brought together eager young minds representing the many facets of cancer care and uniting basic science and the clinic. Attracting a capacity crowd, the evening was a resounding success and provided many young delegates with the ideal opportunity to take their first step towards making a difference together.

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## New data in HCC and mCRC

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**Monday, September 11, at 13:00–14:25**

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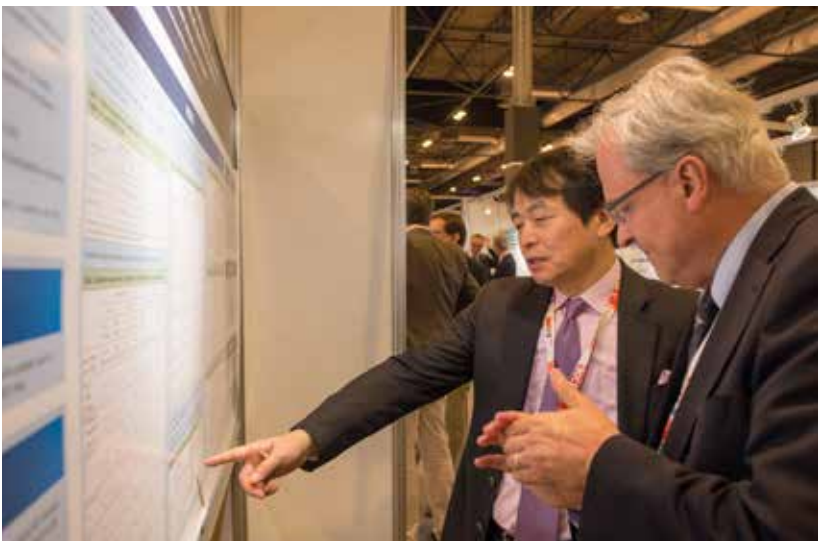
**Chairs: Roberto Cianni (Italy), Eric Van Cutsem (Belgium)**

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# Reportage – Day three






















**Epacadostat:** An investigational, selective oral inhibitor of indoleamine-2,3-dioxygenase 1 (IDO1)

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## The ECHO Clinical Trial Program Is Now Enrolling in Multiple Tumor Types

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	Glioblastoma		Non-small cell lung cancer		Advanced solid tumors

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The efficacy and safety of the investigational compounds discussed have not been established. There is no guarantee that these compounds will become commercially available for the use(s) under investigation.

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