Ludwig Boltzmann Institut
Health Technology Assessment

Horizon Scanning in Oncology
33rd Prioritization – 4th quarter 2017

General Information, efficacy and safety data

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Please note:

Within this document you find general information about the drug of interest and the indication it is intended to be used for. Further we have included full text publications and conference abstracts of phase III trials, assessing the safety and efficacy of the drugs of interest.

At the very end of each chapter we have provided a table containing the prioritization criteria and a drop-down field to apply the provided criteria.

Introduction

As part of the project „Horizon Scanning in Oncology“ (further information can be found here: http://hta.lbg.ac.at/page/horizon-scanning-in-der-onkologie), 9 information sources are scanned frequently to identify emerging anticancer drugs.

Every 3 months, these anticancer therapies are filtered (i.e. in most cases defined as availability of phase III results; for orphan drugs also phase II) to identify drugs at/around the same time as the accompanying drug licensing decisions of the EMA.

An expert panel consisting of oncologists and pharmacists then applies 5 prioritisation criteria to elicit those anti-cancer therapies which might be associated with either a considerable impact on financial resources or a substantial health benefit.

For the 33 prioritisation (October 2017), 9 drugs were filtered out of 401 identified and were sent to prioritisation. Of these, 5 drugs were ranked as ‘highly relevant’ by the expert panel, 4 as ‘relevant’ and none as ‘not relevant’. For ‘highly relevant’ drugs, further information including, for example, abstracts of phase III studies and licensing status is contained in this document.

The summary judgements of the expert panel for all prioritised drugs are provided in the following table.

No	Filtered Drugs – 33rd prioritisation 4th quarter 2017	Overall category
1.	Nivolumab (Opdivo®) in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142)	Highly relevant
2.	Adjuvant nivolumab (Opdivo®) versus ipilimumab in resected stage III or IV melanoma	Relevant
3.	Adjuvant dabrafenib (Tafinlar®) plus trametinib in stage III BRAF-mutated melanoma	Relevant
4.	Avelumab (Bavencio®) in patients with chemotherapy-refractory metastatic Merkel cell carcinoma	Relevant
5.	Durvalumab (Imfinzi™) after chemoradiotherapy in stage III non–small-cell lung cancer	Highly relevant
6.	Brentuximab vedotin (Adcetris®) or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA	Highly relevant
7.	Idelalisib (Zydelig®) or placebo in combination with bendamustine and rituximab in patients with relapsed or refractory chronic lymphocytic leukaemia	Relevant
8.	Midostaurin (Rydapt®) plus chemotherapy for acute myeloid leukemia with a FLT3 mutation	Highly relevant
9.	Abiraterone (Zytiga®) in combination with prednisone androgen-deprivation therapy in metastatic, castration-sensitive prostate cancer	Highly relevant

1 Colorectal cancer

1.1 Nivolumab (Opdivo®) in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142)

Overview

Drug Description		humanized IgG4 anti-PD-1 monoclonal antibody
Patient Indication		nivolumab for metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer
Incidence in Austria		4,567 newly diagnosed per year (2014), 55.0/100,000/year (European Standard Population, 2013)
Ongoing Phase II		NCT02060188 until 2019
Approval status for this indication	**EMA**	-
	FDA	07/2017: for the treatment of patients 12 years and older with mismatch repair deficient (dMMR) and microsatellite instability high (MSI-H) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
Approval status for other indications	**EMA**	02/2016: for the treatment of non-small cell lung cancer (NSCLC) that has spread locally or to other parts of the body in patients who have previously been treated 04/2016: as a monotherapy for advanced renal cell carcinoma in previously treated patients 05/2016: for the treatment of advanced melanoma as a monotherapy or in combination with ipilimumab 10/2016: for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant and treatment with brentuximab vedotin 04/2017: for the treatment of squamous cell cancer of the head and neck (SCCHN) in adults progressing on or after platinum-based therapy for nivolumab as monotherapy 06/2017: for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy for nivolumab
	FDA	09/2015: BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent 09/2015: BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent 09/2015: unresectable or metastatic melanoma, in combination with ipilimumab 10/2015: metastatic non-small cell lung cancer and progression on or after platinum based chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have disease progression on FDA-approved therapy for

		these aberrations prior to receiving OPDIVO 11/2015: advanced renal cell carcinoma who have received prior anti-angiogenic therapy 05/2016: for the treatment of patients with classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation and post-transplantation brentuximab vedotin 11/2016: for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy 02/2017: for the treatment of previously treated locally advanced or metastatic urothelial carcinoma
Costs		Nivolumab 1 treatment cycle: 3 mg/kg intravenously every 2 weeks (assuming an average body weight of 70 kg); ex-factory price of 40 mg = € 572,- → € 6,006,- per treatment cycle

Phase III results

Lancet 2017 July, 18(9):1182-1191 (Overman et al.): *"Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study"*

Background
Metastatic DNA mismatch repair-deficient (dMMR)/microsatellite instability-high (MSI-H) colorectal cancer has a poor prognosis after treatment with conventional chemotherapy and exhibits high levels of tumour neoantigens, tumour-infiltrating lymphocytes, and checkpoint regulators. All of these features are associated with the response to PD-1 blockade in other tumour types. Therefore, we aimed to study nivolumab, a PD-1 immune checkpoint inhibitor, in patients with dMMR/MSI-H metastatic colorectal cancer.

Methods
In this ongoing, multicentre, open-label, phase 2 trial, we enrolled adults (aged ≥18 years) with histologically confirmed recurrent or metastatic colorectal cancer locally assessed as dMMR/MSI-H from 31 sites (academic centres and hospitals) in eight countries (Australia, Belgium, Canada, France, Ireland, Italy, Spain, and the USA). Eligible patients had progressed on or after, or been intolerant of, at least one previous line of treatment, including a fluoropyrimidine and oxaliplatin or irinotecan. Patients were given 3 mg/kg nivolumab every 2 weeks until disease progression, death, unacceptable toxic effects, or withdrawal from study. The primary endpoint was investigator-assessed objective response as per Response Evaluation Criteria in Solid Tumors (version 1.1). All patients who received at least one dose of study drug were included in all analyses. This trial is registered with ClinicalTrials.gov, number NCT02060188.

Findings
Of the 74 patients who were enrolled between March 12, 2014, and March 16, 2016, 40 (54%) had received three or more previous treatments. At a median follow-up of 12·0 months (IQR 8.6–18.0), 23 (31.1%, 95% CI 20.8–42.9) of 74 patients achieved an investigator-assessed objective response and 51 (69%, 57–79) patients had disease control for 12 weeks or longer. Median duration of response was not yet reached; all responders were alive, and eight had responses lasting 12 months or longer (Kaplan-Meier 12-month estimate 86%, 95% CI 62–95). The most common grade 3 or 4 drug-related adverse events were increased concentrations of lipase (six [8%]) and amylase (two [3%]). 23 (31%) patients died during the study; none of these deaths were deemed to be treatment related by the investigator.

Interpretation
Nivolumab provided durable responses and disease control in pre-treated patients with dMMR/MSI-H metastatic colorectal cancer, and could be a new treatment option for these patients.

2 Lung cancer

2.1 Durvalumab (Imfinzi™) after chemoradiotherapy in stage III non–small-cell lung cancer

Overview

Drug Description		programmed death-ligand 1 (PD-L1) blocking antibody
Patient Indication		durvalumab as consolidation therapy in patients with stage III NSCLC who did not have disease progression after two or more cycles of platinum-based chemoradiotherapy
Incidence in Austria		4,716 newly diagnosed per year (2014), 56.9/100,000/year (European Standard Population, 2013)
Ongoing Phase II		NCT02125461 until 2019
Approval status for this indication	**EMA**	-
	FDA	-
Approval status for other indications	**EMA**	-
	FDA	05/2017: for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
Costs		-

Phase III results

NEJM; published online 8 September 2017 (Antonia et al.): *"Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer"*

Background
Most patients with locally advanced, unresectable, non–small-cell lung cancer (NSCLC) have disease progression despite definitive chemoradiotherapy (chemotherapy plus concurrent radiation therapy). This phase 3 study compared the anti–programmed death ligand 1 antibody durvalumab as consolidation therapy with placebo in patients with stage III NSCLC who did not have disease progression after two or more cycles of platinum-based chemoradiotherapy.

Methods
We randomly assigned patients, in a 2:1 ratio, to receive durvalumab (at a dose of 10 mg per kilogram of body weight intravenously) or placebo every 2 weeks for up to 12 months. The study drug was administered 1 to 42 days after the patients had received chemoradiotherapy. The coprimary end points were progression-free survival (as assessed by means of blinded independent central review) and overall survival (unplanned for the interim analysis). Secondary end points included 12-month and 18-month progression-free survival rates, the objective response rate, the duration of response, the time to death or distant metastasis, and safety.

Results
Of 713 patients who underwent randomization, 709 received consolidation therapy (473 received durvalumab and 236 received placebo). The median progression-free survival from randomization was 16.8 months (95% confidence interval [CI], 13.0 to 18.1) with durvalumab versus 5.6 months (95% CI,

4.6 to 7.8) with placebo (stratified hazard ratio for disease progression or death, 0.52; 95% CI, 0.42 to 0.65; P<0.001); the 12-month progression-free survival rate was 55.9% versus 35.3%, and the 18-month progression-free survival rate was 44.2% versus 27.0%. The response rate was higher with durvalumab than with placebo (28.4% vs. 16.0%; P<0.001), and the median duration of response was longer (72.8% vs. 46.8% of the patients had an ongoing response at 18 months). The median time to death or distant metastasis was longer with durvalumab than with placebo (23.2 months vs. 14.6 months; P<0.001). Grade 3 or 4 adverse events occurred in 29.9% of the patients who received durvalumab and 26.1% of those who received placebo; the most common adverse event of grade 3 or 4 was pneumonia (4.4% and 3.8%, respectively). A total of 15.4% of patients in the durvalumab group and 9.8% of those in the placebo group discontinued the study drug because of adverse events.

Conclusions
Progression-free survival was significantly longer with durvalumab than with placebo. The secondary end points also favored durvalumab, and safety was similar between the groups. (Funded by AstraZeneca; PACIFIC ClinicalTrials.gov number, NCT02125461.)

3 Lymphoma

3.1 Brentuximab vedotin (Adcetris®) or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA)

Overview

Drug Description		is an antibody-drug conjugate (ADC) directed to the protein CD30
Patient Indication		brentuximab vedotin in previously treated patients with CD30-positive cutaneous T-cell lymphomas
Incidence in Austria		1,272 newly diagnosed per year (2014), 15.3/100,000/year (European Standard Population, 2013)
Ongoing Phase II		-
Approval status for this indication	**EMA**	-
	FDA	The FDA granted Priority Review for Brentuximab vedotin in CD30-positive cutaneous T-cell lymphoma.
Approval status for other indications	**EMA**	10/2012: Adcetris is indicated for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL): • following autologous stem-cell transplant (ASCT) or; • following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. Adcetris is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large-cell lymphoma (sALCL). 06/2016: Adcetris is indicated for the treatment of adult patients with CD30+ HL at increased risk of relapse or progression following ASCT.
	FDA	08/2011: for the treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates. 08/2011: for the treatment of patients with systemic anaplastic large cell lymphoma (ALCL) after failure of at least one prior multi-agent chemotherapy regimen
Costs		Brentuximab vedotin: 1 treatment cycle → 1.8 mg/kg once every 3 weeks (assuming an average body weight of 70 kg); ex-factory price of 50 mg = € 3,333.00,- → € 8,399.16,- per treatment cycle

Phase III results

Lancet 2017 August, 390(10094):555-566 (Prince et al.): *"Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial"*

Background
Cutaneous T-cell lymphomas are rare, generally incurable, and associated with reduced quality of life. Present systemic therapies rarely provide reliable and durable responses. We aimed to assess

efficacy and safety of brentuximab vedotin versus conventional therapy for previously treated patients with CD30-positive cutaneous T-cell lymphomas.

Methods
In this international, open-label, randomised, phase 3, multicentre trial, we enrolled adult patients with CD30-positive mycosis fungoides or primary cutaneous anaplastic large-cell lymphoma who had been previously treated. Patients were enrolled across 52 centres in 13 countries. Patients were randomly assigned (1:1) centrally by an interactive voice and web response system to receive intravenous brentuximab vedotin 1.8 mg/kg once every 3 weeks, for up to 16.3-week cycles, or physician's choice (oral methotrexate 5–50 mg once per week or oral bexarotene 300 mg/m^2 once per day) for up to 48 weeks. The primary endpoint was the proportion of patients in the intention-to-treat population achieving an objective global response lasting at least 4 months per independent review facility. Safety analyses were done in all patients who received at least one dose of study drug. This trial was registered with ClinicalTrials.gov, number NCT01578499.

Findings
Between Aug 13, 2012, and July 31, 2015, 131 patients were enrolled and randomly assigned to a group (66 to brentuximab vedotin and 65 to physician's choice), with 128 analysed in the intention-to-treat population (64 in each group). At a median follow-up of 22.9 months (95% CI 18.4–26.1), the proportion of patients achieving an objective global response lasting at least 4 months was 56·3% (36 of 64 patients) with brentuximab vedotin versus 12·5% (eight of 64) with physician's choice, resulting in a between-group difference of 43·8% (95% CI 29.1–58.4; p<0·0001). Grade 3–4 adverse events were reported in 27 (41%) of 66 patients in the brentuximab vedotin group and 29 (47%) of 62 patients in the physician's choice group. Peripheral neuropathy was seen in 44 (67%) of 66 patients in the brentuximab vedotin group (n=21 grade 2, n=6 grade 3) and four (6%) of 62 patients in the physician's choice group. One of the four on-treatment deaths was deemed by the investigator to be treatment-related in the brentuximab vedotin group; no on-treatment deaths were reported in the physician's choice group.

Interpretation
Significant improvement in objective response lasting at least 4 months was seen with brentuximab vedotin versus physician's choice of methotrexate or bexarotene.

4 Leukaemia

4.1 Midostaurin (Rydapt®) plus chemotherapy for acute myeloid leukemia with a FLT3 mutation

Overview

Drug Description		a small molecule that inhibits multiple receptor tyrosine kinases
Patient Indication		midostaurin in combination to standard chemotherapy in patients with acute myeloid leukemia and a FLT3 mutation
Incidence in Austria		936 newly diagnosed per year (2014), 11.3/100,000/year (European Standard Population, 2013)
Ongoing Phase II		-
Approval status for this indication	**EMA**	On 20 July 2017, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Rydapt, intended for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are FLT3 mutation-positive and for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM AHN), or mast cell leukaemia (MCL). Rydapt was designated as an orphan medicinal product on 29 July 2004
	FDA	04/2017: for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive (FLT3+), as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.
Approval status for other indications	**EMA**	08/2010, orphan designation was granted by the European Commission to Novartis Europharm Limited, United Kingdom, for midostaurin for the treatment of mastocytosis.
	FDA	04/2017: midostaurin for the treatment of adults with aggressive systemic mastocytosis (SM), SM with associated hematological neoplasm, or mast cell leukemia.
Costs		-

Phase III results

Lancet published online June 2017, (Stone et al.) *"Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation"*

Background
Patients with acute myeloid leukemia (AML) and a *FLT3* mutation have poor outcomes. We conducted a phase 3 trial to determine whether the addition of midostaurin — an oral multitargeted kinase inhibitor that is active in patients with a *FLT3* mutation — to standard chemotherapy would prolong overall survival in this population.

Methods
We screened 3277 patients, 18 to 59 years of age, who had newly diagnosed AML for *FLT3* mutations. Patients were randomly assigned to receive standard chemotherapy (induction therapy with daunorubicin and cytarabine and consolidation therapy with high-dose cytarabine) plus either midostaurin or placebo; those who were in remission after consolidation therapy entered a maintenance phase in which they received either midostaurin or placebo. Randomization was stratified according to subtype of *FLT3* mutation: point mutation in the tyrosine kinase domain (TKD) or internal

tandem duplication (ITD) mutation with either a high ratio (>0.7) or a low ratio (0.05 to 0.7) of mutant to wild-type alleles (ITD [high] and ITD [low], respectively). Allogeneic transplantation was allowed. The primary end point was overall survival.

Results
A total of 717 patients underwent randomization; 360 were assigned to the midostaurin group, and 357 to the placebo group. The *FLT3* subtype was ITD (high) in 214 patients, ITD (low) in 341 patients, and TKD in 162 patients. The treatment groups were well balanced with respect to age, race, *FLT3* subtype, cytogenetic risk, and blood counts but not with respect to sex (51.7% in the midostaurin group vs. 59.4% in the placebo group were women, P = 0.04). Overall survival was significantly longer in the midostaurin group than in the placebo group (hazard ratio for death, 0.78; one-sided P = 0.009), as was event-free survival (hazard ratio for event or death, 0.78; one-sided P = 0.002). In both the primary analysis and an analysis in which data for patients who underwent transplantation were censored, the benefit of midostaurin was consistent across all *FLT3* subtypes. The rate of severe adverse events was similar in the two groups.

Conclusions
The addition of the multitargeted kinase inhibitor midostaurin to standard chemotherapy significantly prolonged overall and event-free survival among patients with AML and a *FLT3* mutation. (Funded by the National Cancer Institute and Novartis; ClinicalTrials.gov number, NCT00651261.)

5 Prostate caner

5.1 Abiraterone (Zytiga®) in combination with prednisone androgen-deprivation therapy in metastatic, castration-sensitive prostate cancer

Overview

Drug Description		an androgen biosynthesis inhibitor, that inhibits 17 α-hydroxylase/C17,20-lyase (CYP17)
Patient Indication		Abiraterone in combination with prednisone androgen-deprivation therapy in metastatic, castration-sensitive prostate cancer
Incidence in Austria		4,499 newly diagnosed per year (2014), 124.0/100,000/year (European Standard Population, 2013)
Ongoing Phase II		NCT00268476 until 2017 NCT01715285 until 2021
Approval status for this indication	**EMA**	-
	FDA	-
Approval status for other indications	**EMA**	09/2011: in combination with prednisone or prednisolone for the treatment of metastatic castration resistant prostate cancer in adult men whose disease has progressed on or after a docetaxel based chemotherapy regimen. 12/2012: in combination with prednisone or prednisolone for the treatment of metastatic castration resistant prostate cancer in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.
	FDA	04/2011: in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.
Costs		Abiraterone: 1,000 mg orally (given once daily as four 250-mg tablets); ex-factory price of 28,000 mg = € 2,895.35,- → € 2,171.51 for 21 days of treatment

Phase III results

NEJM published online June 2017 (Fizazi et al.) *"Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer"*

Background
Abiraterone acetate, a drug that blocks endogenous androgen synthesis, plus prednisone is indicated for metastatic castration-resistant prostate cancer. We evaluated the clinical benefit of abiraterone acetate plus prednisone with androgen-deprivation therapy in patients with newly diagnosed, metastatic, castration-sensitive prostate cancer.
Methods
In this double-blind, placebo-controlled, phase 3 trial, we randomly assigned 1199 patients to receive either androgen-deprivation therapy plus abiraterone acetate (1000 mg daily, given once daily as four 250-mg tablets) plus prednisone (5 mg daily) (the abiraterone group) or androgen-deprivation therapy plus dual placebos (the placebo group). The two primary end points were overall survival and radiographic progression-free survival.
Results
After a median follow-up of 30.4 months at a planned interim analysis (after 406 patients had died), the median overall survival was significantly longer in the abiraterone group than in the placebo group (not

reached vs. 34.7 months) (hazard ratio for death, 0.62; 95% confidence interval [CI], 0.51 to 0.76; P<0.001). The median length of radiographic progression-free survival was 33.0 months in the abiraterone group and 14.8 months in the placebo group (hazard ratio for disease progression or death, 0.47; 95% CI, 0.39 to 0.55; P<0.001). Significantly better outcomes in all secondary end points were observed in the abiraterone group, including the time until pain progression, next subsequent therapy for prostate cancer, initiation of chemotherapy, and prostatespecific antigen progression (P<0.001 for all comparisons), along with next symptomatic skeletal events (P = 0.009). These findings led to the unanimous recommendation by the independent data and safety monitoring committee that the trial be unblended and crossover be allowed for patients in the placebo group to receive abiraterone. Rates of grade 3 hypertension and hypokalemia were higher in the abiraterone group.

Conclusion
The addition of abiraterone acetate and prednisone to androgen-deprivation therapy significantly increased overall survival and radiographic progression-free survival in men with newly diagnosed, metastatic, castration-sensitive prostate cancer. (Funded by Janssen Research and Development; LATITUDE ClinicalTrials.gov number, NCT01715285.)

NEJM published online June 2017 (James et al.) *"Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy"*

Background
Abiraterone acetate plus prednisolone improves survival in men with relapsed prostate cancer. We assessed the effect of this combination in men starting long-term androgen-deprivation therapy (ADT), using a multigroup, multistage trial design.

Methods
We randomly assigned patients in a 1:1 ratio to receive ADT alone or ADT plus abiraterone acetate (1000 mg daily) and prednisolone (5 mg daily) (combination therapy). Local radiotherapy was mandated for patients with node-negative, nonmetastatic disease and encouraged for those with positive nodes. For patients with nonmetastatic disease with no radiotherapy planned and for patients with metastatic disease, treatment continued until radiologic, clinical, or prostate-specific antigen (PSA) progression; otherwise, treatment was to continue for 2 years or until any type of progression, whichever came first. The primary outcome measure was overall survival. The intermediate primary outcome was failure-free survival (treatment failure was defined as radiologic, clinical, or PSA progression or death from prostate cancer).

Results
A total of 1917 patients underwent randomization from November 2011 through January 2014. The median age was 67 years, and the median PSA level was 53 ng per milliliter. A total of 52% of the patients had metastatic disease, 20% had node-positive or node-indeterminate nonmetastatic disease, and 28% had node-negative, nonmetastatic disease; 95% had newly diagnosed disease. The median follow-up was 40 months. There were 184 deaths in the combination group as compared with 262 in the ADT-alone group (hazard ratio, 0.63; 95% confidence interval [CI], 0.52 to 0.76; P<0.001); the hazard ratio was 0.75 in patients with nonmetastatic disease and 0.61 in those with metastatic disease. There were 248 treatment-failure events in the combination group as compared with 535 in the ADT-alone group (hazard ratio, 0.29; 95% CI, 0.25 to 0.34; P<0.001); the hazard ratio was 0.21 in patients with nonmetastatic disease and 0.31 in those with metastatic disease. Grade 3 to 5 adverse events occurred in 47% of the patients in the combination group (with nine grade 5 events) and in 33% of the patients in the ADT-alone group (with three grade 5 events).

Conclusion
Among men with locally advanced or metastatic prostate cancer, ADT plus abiraterone and prednisolone was associated with significantly higher rates of overall and failure-free survival than ADT alone. (Funded by Cancer Research U.K. and others; STAMPEDE ClinicalTrials.gov number, NCT00268476, and Current Controlled Trials number, ISRCTN78818544.)