Evaluate Vantage

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Esmo preview – Immuno-oncology and beyond

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As the European Society of Medical Oncology, Europe's answer to Asco, unveiled the abstracts to be presented at its annual congress today it was clear that PD-1/PD-L1 inhibition is set to be one of the meeting's key themes.

Plenty of other developments are hotly awaited too, including more on the Mek/Braf inhibition landscape, the continued battle between Clovis and AstraZeneca in mutated lung cancer, and the Parp inhibitor class. But Checkmate-037, the first randomised phase III trial of a PD-1 inhibitor, Astra's MEDI4736 plus tremelimumab, and PD-1/PD-L1 blockade in additional tumour types will likely generate the most investor excitement.

Data from Checkmate-037, a study of Bristol-Myers Squibb's nivolumab – recently approved in Japan as Opdivo – in melanoma, are being kept back in a late-breaker for presentation on September 29 at the presidential symposium, Esmo's equivalent of a plenary session. The trial is the basis for Opdivo's US filing, and response rate and durability will be a point of focus.

Merck & Co's pembrolizumab (Keytruda) beat Opdivo to the US market, and will feature in five late-breaking abstracts. Among the most interesting will be its first data in gastric and bladder cancers; Roche's data for MPDL3280A in metastatic urothelial bladder cancer was one of the highlight's of May's Asco meeting.

An update on the MPDL3280A bladder cancer study is also expected, as well as data from a combination of this anti-PD-L1 antibody with Avastin. However, both are proffered papers, whose text is being kept under wraps until September 24.

Meanwhile, one of the highlights of the abstracts revealed today is a phase I NSCLC study of Astra's MEDI4736 plus tremelimumab. Two of 12 patients have dropped out of the trial owing to adverse events – increased liver enzymes, myasthenia gravis and colitis – and there have been two unconfirmed partial responses; these early findings might prompt concerns.

Braf advantage

Also featured at the presidential session on September 29 will be the phase III trials Combi-v, of GlaxoSmithKline/Novartis's Tafinlar plus Mekinist, and CoBRIM, of Roche/Exelixis's Zelboraf plus cobimetinib.

Advantage in this combination approach to treating Braf-mutated melanoma has swung away from Roche and Exelixis, so the additional data will be closely watched (*Glaxo's Mek/Braf combo spoils the Exelixis party, July 18, 2014*). Already 2014 has turned into an annus horribilis for Exelixis, with its other key asset, Cometriq, failing in prostate cancer.

A phase III trial of Novartis's Mek inhibitor binimetinib in Nras-mutated melanoma is also the subject of a late-breaker, but the return of this asset to its originator, Array Biopharma, is a near certainty.

One failure revealed in today's abstracts is that of Gilead's simtuzumab in pancreatic cancer. In a 236-patient phase II trial adding simtuzumab to gemcitabine failed to prolong progression-free or overall survival, though analysts were not holding out much hope, and simtuzumab's far more important potential use lies in non-alcoholic steatohepatitis.

Interestingly, another failed study – Magrit, featuring Glaxo's MAGE-A3 cancer vaccine – will be discussed at the presidential symposium on September 28; presumably this could provide general clues to immunotherapy.

Parp competition

Despite a recent US advisory panel vote against approving Astra's olaparib, other Parp inhibitors will play important roles at Esmo. Clovis's rucaparib, for instance, is being studied in Ariel2, a phase I/II ovarian cancer study; data from 103 patients show some additional activity in patients without the BRCA mutation – responses that will inform the ongoing Ariel3 phase III study.

Meanwhile, AbbVie's veliparib has failed to show a significant improvement in survival in metastatic NSCLC

when combined with chemotherapy, but based on promise in squamous tumours a phase III study in patients with this histology is ongoing. A phase III trial of Tesaro's niraparib in platinum-sensitive recurrent ovarian cancer is also under way.

And a host of other small biotechs will look to Esmo to provide investment catalysts. Ariad, for instance, is presenting phase II data for AP26113, increasingly seen as its main driver, showing a 69% response in Alk-positive NSCLC patients resistant to Pfizer's Xalkori.

A phase I study of Ignyta's Alk-inhibitor RXDX-101 will be presented, showing good tolerability. Endocyte's long-suffering investors will hope for overall survival data from vintafolide's phase II Target study.

Oncomed, another small-cap stock that has underperformed this year, will highlight phase I tolerability data for demcizumab and tarextumab; these are under option to Celgene and GlaxoSmithKline respectively, while a third project, vanticumab, recently had its US phase I hold lifted.

Esmo will also focus on the fast-moving and highly competitive prostate cancer space, with Johnson & Johnson presenting an update on a study of ARN-509 showing a 48% PSA response at 36 weeks. Spartan, a phase III trial, continues.

ODM-201, a rival androgen receptor antagonist from Bayer/Orion, is also in phase III, and its Esmo data are limited to a retrospective analysis of the phase I/II Arades trial. Medivation's Xtandi still has a stranglehold on this space and remains the agent to beat.

Medivation had a strong Asco, and its competitors, along with many other large and small oncology players, will rely on Esmo to build on data presented in Chicago in May.

Selected presentations at 2014 Esmo meeting			
Project	**Company**	**Study name**	**Trial ID**
Opdivo	Bristol-Myers Squibb	Checkmate-037	NCT01721746
Keytruda	Merck & Co	Keynote-12	NCT01848834
MPDL3280A + Avastin	Roche	–	NCT01984242
MEDI4736 + tremelimumab	AstraZeneca	D4190C00006	NCT02000947
Tafinlar + Mekinist	Glaxo/Novartis	Combi-v	NCT01597908
Zelboraf + cobimetinib	Roche/Exelixis	CoBRIM	NCT01689519
Iressa	AstraZeneca	Impress	NCT01544179
AZD9291	AstraZeneca	Aura	NCT01802632
Neratinib	Puma	–	NCT01827267
Vintafolide	Endocyte	Target	NCT01577654
Binimetinib	Novartis/Array	–	NCT01320085
Simtuzumab	Gilead	–	NCT01472198
Mage-A3	GlaxoSmithKline	Magrit	NCT00480025
Rucaparib	Clovis Oncology	Ariel2	NCT01891344
Olaparib	AstraZeneca	Toparp	NCT01682772
Veliparib	AbbVie	–	NCT01560104
AP26113	Ariad	–	NCT01449461
RXDX-101	Ignyta	Startrk-1	NCT02097810
Demcizumab	Oncomed	–	NCT01189929
Tarextumab	Oncomed	Alpine	NCT01647828
ARN-509	Johnson & Johnson	ARN-509-001	NCT01171898
ODM-201	Bayer/Orion	Arades	NCT01317641

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