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Go or no go? FDA firsts for Imfinzi, Enhertu and roflumilast

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Assets in oncology and psoriasis are set for upcoming Pdufa decisions.

As the summer months roll on, Astrazeneca's Imfinzi could become the first immunotherapy approved in front-line biliary tract cancer, an area lacking treatment options, while Enhertu could be heading for Her2-mutant lung cancer.

Elsewhere, Arcutis could win its first ever green light; the FDA is due to decide on roflumilast, a topical PDE4 inhibitor in psoriasis, by the end of next month.

Oncology firsts

Imfinzi is the first immunotherapy to prevail in first-line biliary tract cancer, albeit with underwhelming data. Despite this, a lack of options in front-line disease could sway the US regulator, and a decision is due in the third quarter.

At this year's Asco-GI conference data from Topaz-1 showed that Imfinzi plus chemo reduced the risk of death by 20% versus chemo alone. Median overall survival was just 1.3 months longer than in the control arm, however.

This tumour type has seen approvals of Incyte's Pemazyre and Bridgebio's Truseltiq, both in FGFR2-mutant disease, and Agios's Tibsovo in IDH1-mutant disease, all in a second-line setting.

Other anti-PD-(L)1 inhibitors are in front-line studies: the phase 3 Keynote-966 trial is evaluating Merck & Co's Keytruda plus chemo, with overall survival as the primary endpoint; Roche's Tecentriq is being given with chemo, plus or minus Avastin, in the phase 2 Imbrave-151 study. Progression-free survival is the primary measure in the latter, and both are due to complete next year.

Meanwhile, Daiichi Sankyo and Astrazeneca's Enhertu could become the first Her2-targeted agent in lung cancer in the third quarter. The filing was based on the Destiny-Lung01 study that showed an impressive 55% response rate in a late-line population, as reported at last year's Esmo.

But the issue of interstitial lung disease again raised its head: among 91 patients, ILD caused two deaths and an almost 30% discontinuation rate. However, patients had a median of two prior treatments, with some having had seven – clearly an advanced group who, according to the investigators, might be expected to suffer high rates of ILD.

A first-line lung study, Destiny-Lung04, is already under way. Lung cancer is likely a small opportunity for Enhertu, with 2028 forecasts of $511m, compared with $5.6bn in breast cancer.

Getting topical

The PDE4 inhibitor roflumilast has been around for over a decade as an oral therapy in COPD, but now Arcutis could get the first topical version approved in plaque psoriasis by July 29.

The psoriasis market is crowded with injectable biologics for moderate-to-severe disease, but the current standard of care for most patients is corticosteroids. These come with side effects such as thinning skin, and are not recommended for long-term use.

Arcutis completed two twin phase 3 studies in patients aged 2 or over with mild-to-moderate psoriasis. Dermis-1 and 2 each achieved the primary efficacy endpoint of investigator global assessment success at week eight versus vehicle cream. The most noticeable side effect with treatment was diarrhoea, a well-known issue with PDE4 inhibitors; however, cases were transient and mostly mild.

Arcutis has pointed out that its 8-week efficacy data are comparable to 12-week data with Dermavant's topical therapy Vtama, an aryl hydrocarbon receptor agonist recently FDA approved for all disease severities. On the measure of psoriasis area severity index-75, Arcutis has also noted that its data at 8 weeks surpass 16-week data for Otezla, Amgen's oral PDE4 inhibitor.

The tables below lists first-time and supplementary US approval decisions due next month, with consensus forecasts from *Evaluate Pharma.*

Notable first-time US approval decisions due in July

Project	Company	Pdufa date	Indication(s)	2028e sales by indication (SBI) ($m)	Note
Tislelizumab	Beigene/Novartis	July 12	2nd-line oesophageal squamous cell carcinoma	83	Filing based on global Rationale-302 study (*China-backed US approvals continue to hang in the balance*)
Zonisamide oral suspension	Eton	July 18	Partial seizures in patients with epilepsy	-	Several delays already, last one in January owing to outstanding onsite FDA inspection
Roflumilast cream	Arcutis/ Astrazeneca	July 29	Plaque psoriasis	606	Topical PDE4 inhibitor
Ryzneuta	Evive Biotech (private)	Pending	Chemotherapy-induced neutropenia	-	-
SH-111	Shorla Oncology (private)	Pending	T-cell leukaemia	-	-
AXS-05	Axsome	Pending	Major depressive disorder	787	Company disclosed in June that it was in FDA labelling discussions
Annik (penpulimab)	Akeso/Sino	Pending (was estimated as H1)	3L nasopharyngeal carcinoma	-	*China-backed US approvals continue to hang in the balance*

Source: company releases & Evaluate Pharma.

Supplementary and other notable approval decisions due in July			
Product	**Company**	**Indication (clinical trial)**	**Date**
Krystexxa + methotrexate	Horizon	Uncontrolled gout (Mirror)	July 7
Ronapreve (Regen-Cov)	Regeneron	Covid in non-hospitalised patients and as prophylaxis in certain individuals (EUA in Nov 2020, limited Jan 22 owing to omicron variant) (NCT04425629, NCT04452318)	July 13
Opzelura (ruxolitinib cream)	Incyte	Adolescents and adults with vitiligo (True-V1, True-V2)	July 18
Imfinzi + chemo	Astrazeneca	1L biliary tract cancer (Topaz-1)	Q3
Enhertu	Astra/Daiichi Sankyo	2L Her2-positive NSCLC (Destiny-Lung01)	Q3
Actemra	Roche	Hospitalised Covid patients (EUA in June 2021) (Empacta, Covacta, Remdacta, Recovery)	H2
Source: company releases & Evaluate Pharma.			