Evaluate Vantage

February 17, 2021

Lynparza’s Olympia win could broaden breast cancer use

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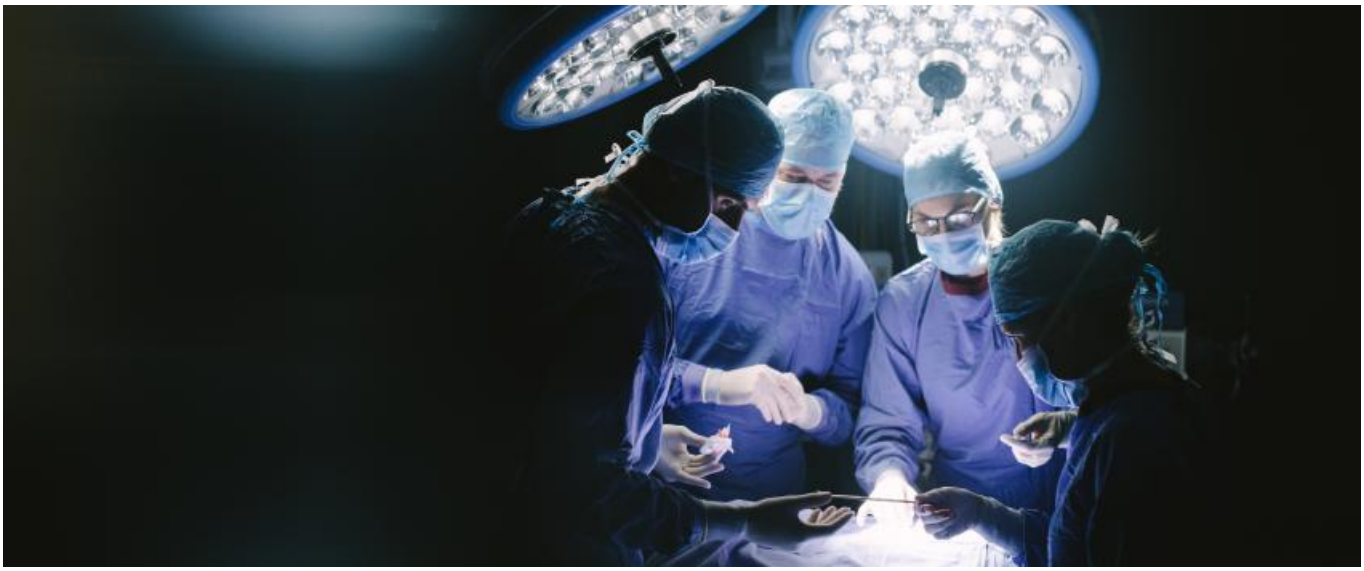

The Parp inhibitor registers an unexpected clinical win in the adjuvant setting, but more convincing data might still be needed.

An unexpected early breast cancer win in a little-noticed clinical trial could give Astrazeneca/Merck & Co’s Lynparza another edge over its Parp inhibitor rivals, in particular Pfizer’s Talzenna, the only other Parp with breast cancer already on its label.

The Olympia study tested Lynparza against placebo in the adjuvant setting. It had been delayed after having its design overhauled, and some analysts suggested that it was not testing patients sufficiently sensitive to Parp inhibition, but nevertheless it was today halted early for efficacy.

The trial's interim analysis showed that a superiority boundary for its primary endpoint, invasive disease-free survival, had been crossed, and accordingly the full data will now be analysed.

However, Astra’s statement on Olympia cautiously avoids mentioning regulatory plans, though it says Lynparza’s effect was clinically relevant. Whether the benefit translates into a hit on overall survival, a secondary endpoint, is anybody’s guess, and it will take several years’ follow-up before these more robust data mature.

Nevertheless, the signs are good. Lynparza was, of course, the first Parp to succeed in breast cancer in the metastatic setting, its 2017 win in the Olympiad trial leading to US approval a year later for post-chemo use in germline Brca-mutated, Her2-negative disease. The only other Parp with a similar label is Talzenna, which was approved later in 2018 backed by the Embraca trial.

But, perhaps surprisingly, Parps have struggled to make further headway into breast cancer: in the metastatic setting Abbvie’s veliparib disappointed in Brocade-3, while Sanofi’s now discontinued iniparib failed in phase III and was later deemed not to be a true Parp.

Even though Talzenna showed a benefit in a small phase I neoadjuvant study, Pfizer terminated a phase II neoadjuvant trial citing a change in strategy. Most ongoing perioperative studies are in the neoadjuvant setting and are not company-sponsored.

Parp inhibitors in (neo)adjuvant breast cancer trials		
Drug	**Approved for**	**Perioperative breast cancer studies**
Lynparza, Astrazeneca	Ovarian, breast, pancreatic & prostate cancers	Olympia (ph3 adjuvant Her2-ve disease); also academic neoadjuvant trials
Talzenna, Pfizer	Breast cancer	Pfizer terminated NCT03499353 (ph2 neoadjuvant Her2-ve disease); also academic trials
Rubraca, Clovis	Ovarian & prostate cancers	NCT03542175 (ph1 academic-sponsored neoadjuvant trial in TNBC)
Zejula, Glaxosmithkline	Ovarian cancer	NCT04584255 (ph2 dostarlimab combo, academic-sponsored neoadjuvant trial in Her2-ve disease)
Veliparib, Abbvie	NA*	Failed ph3 Brightness trial in neoadjuvant TNBC; also ph1 academic trial
*Note: *veliparib is not approved, and underwhelmed in the metastatic Brocade-3 study. Source: clinicaltrials.gov & company reports.*		

This makes Astra's Olympia success all the more remarkable. This trial had in fact begun enrolling only triple-negative patients, but was later broadened to include those who were ER-positive but still Her2-negative.

It will be interesting to see whether any subgroup drove the benefit, especially as Jefferies analysts had earlier written that ER-positive patients with high-risk features might be insufficiently sensitive to Parp inhibition on account of many of them having residual disease after neoadjuvant chemotherapy.

The analysts also cautioned that without more robust data doctors might be reluctant to prescribe a Parp in the adjuvant breast cancer setting, knowing that the PFS effect in the metastatic Olympiad and Embraca trials had failed to translate into an OS benefit.

Still, perioperative breast cancer settings represent a significant opportunity. *EvaluatePharma's* sales by indication forecasts see breast cancer accounting for just 10% of Lynparza's sellside consensus 2026 revenue of $4.6bn, but this likely only considers the late-line metastatic setting.

Jefferies reckons the adjuvant opportunity is three times bigger than front-line use, which naturally is larger than later-line settings. Astra might still need more data, but with the competition still in early academic trials it does at least have a strong head-start.