

03 Jun 2023 | Analysis

ASCO 2023 – A Role For Immuno-Oncology In Ovarian Cancer At Last?

by

AstraZeneca's Duo-O trial suggests that excluding Brca-positive patients could be the key to Imfinzi's apparent success in ovarian cancer.

[AstraZeneca PLC](#) appears to have teased out a positive result for Imfinzi in ovarian cancer – a setting that so far has proved intractable for anti-PD-(L)1 drugs. The data, toplined positive in April, concern the Duo-O study of an Avastin/Imfinzi/Lynparza triplet, and have been presented 3 June as an American Society of Clinical Oncology (ASCO) late-breaker.

The result is notable for having apparently succeeded where other PD-(L)1/Parp inhibitor combinations have failed, and one reason for this might be Astra's exclusion of Brca-positive patients, who would normally be expected to do well on Avastin/Lynparza alone. Still, questions will remain about Imfinzi's contribution, the breadth of the effect, and the robustness of a progression-free survival endpoint.

Debate continues about the validity of PFS in ovarian cancer, and there have been cases where a clinical benefit on PFS has been followed by a clearly negative result in terms of overall survival. This has, for instance, seen use of [GSK's Parp inhibitor, Zejula, narrowed in ovarian cancer maintenance](#).

Complexities

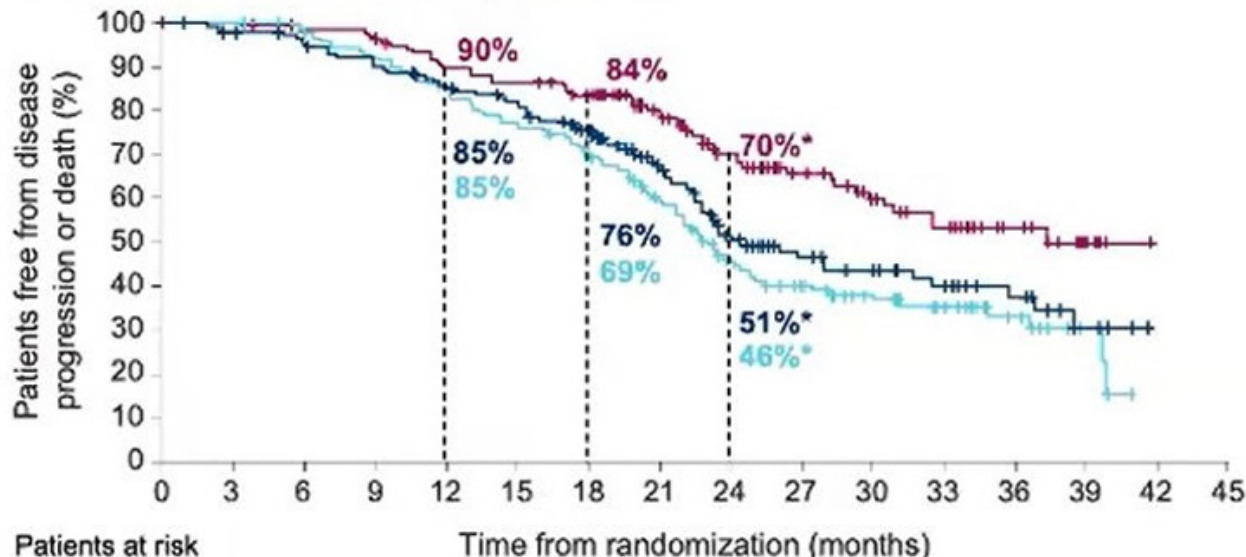
Duo-O had a complex three-arm design, and included two settings. Active cohorts comprised chemo/Avastin/Imfinzi first line followed by Avastin/Imfinzi with or without Lynparza in the maintenance setting; this was compared against a control cohort of chemo/Avastin followed by Avastin maintenance.

A further crucial twist is that the trial enrolled Brca-negative patients only, and its PFS endpoint was split between two co-primaries: an effect in all-comers, and in Brca-negatives who were nevertheless positive for [some other type of HRD mutation](#).

The good news is that the Avastin/Imfinzi/Lynparza maintenance triplet met both co-primaries, with $p < 0.0001$. The bad that Avastin/Imfinzi had no advantage over control at all.

The survival curves reveal another nuance. It might have been assumed that HRD-positive patients are driving the all-comers benefit, but in fact in HRD-negatives, some 60% of the Duo-O Brca-negative population, the triplet also beat control.

Non-tBRCAm HRD-positive

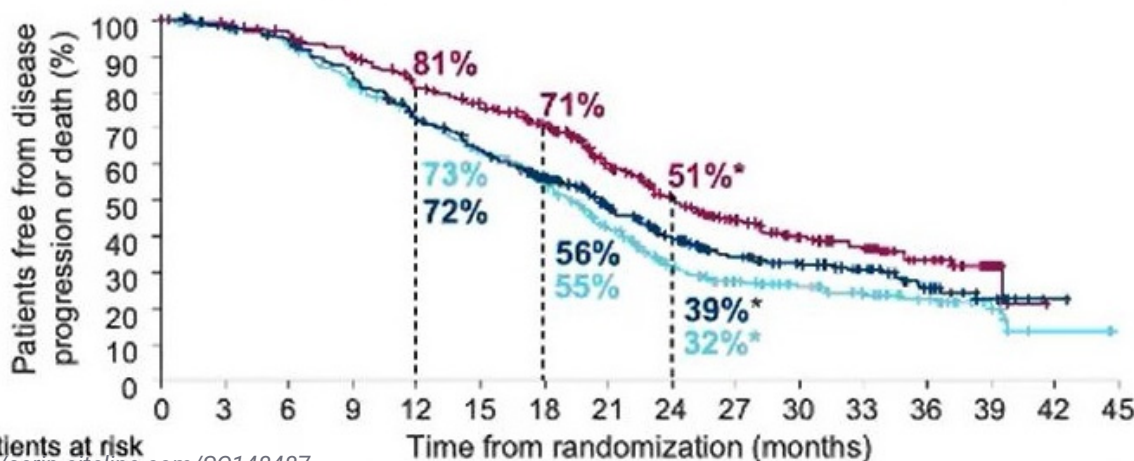


Patients at risk

	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0	0
Arm 2	148	142	137	128	118	112	94	66	45	34	28	21	15	7	0	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0	0

	Arm 1 PC + bev N=143	Arm 2 PC + bev + durva N=148	Arm 3 PC + bev + durva + ola N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, months†	23.0	24.4‡	37.3‡
HR (95% CI) vs Arm 1		0.82 (0.60–1.12)§	0.51 (0.36–0.72)§

Non-tBRCAm ITT



Patients at risk

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	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 2	374	354	336	301	254	221	180	130	93	70	54	39	23	11	1	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	0

PD-(L)1 + Parp inhibition in ovarian cancer					
<i>Roche</i>					
<u>WO39409*</u>	≥2L	Tecentriq + Rubraca	Uncontrolled	Ended 2020 after Covid-related protocol amendment, no data reported	None in ovarian cancer cohort
<i>Merck KGaA/Pfizer</i>					
<u>Javelin Ovarian Parp 100</u>	1L & maintenance	Chemo + Bavencio, then Bavencio + Talzenna	Chemo +/- Avastin, then Talzenna or Avastin	<u>Discontinued after failure of Javelin Ovarian 100 trial</u>	None evident
<i>Merck & Co and/or Astrazeneca</i>					
<u>Duo-O</u>	1L & maintenance	Chemo + Avastin + Imfinzi, then Avastin + Imfinzi +/- Lynparza	Chemo + Avastin, then Avastin	Maintenance triplet positive for PFS in HRD+ves, all-comers & HRD-ves	Must be Brca-ve (including other HRD+ves)
<u>Keylynk-001</u>	1L & maintenance	Chemo + Keytruda, then Lynparza	Chemo +/- Keytruda, then placebo	PFS in PD-L1+ves & all-comers are co-primaries**; ends Oct 2023	Must be Brca-ve
<i>Bristol Myers Squibb/Pharma& (ex Clovis)</i>					

PD-(L)1 + Parp inhibition in ovarian cancer

<u>Athena-Combo</u>	1L maintenance	Opdivo + Rubraca	Opdivo or Rubraca or placebo	PFS primary, data were due Q1 2023***	None evident
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*Note: *not phase 3; **earlier PFS & OS were co-primaries; ***forecast made by Clovis, which later entered bankruptcy and sold Rubraca to Pharma& for \$70m. Source: company statements & clinicaltrials.gov.*

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This article originally appeared in [Evaluate Vantage](#). Evaluate Vantage and Scrip are part of the same parent company, Norstella.