Olaparib

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Approved indication: ovarian cancer

Lynparza (AstraZeneca)
50 mg capsules

Olaparib is indicated as maintenance therapy for people with BRCA-mutated high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer. It is a poly (ADP-ribose) polymerase (PARP) inhibitor. In normal cells, DNA repair during cell division involves BRCA1 and BRCA2 proteins. In people who have mutations in BRCA1 and BRCA2 genes, DNA repair is mediated through alternative pathways and involves PARP enzymes. As olaparib inhibits PARP enzymes, it prevents DNA repair and causes the cancer cells to die.

Olaparib (400 mg twice daily) has been compared to placebo in a phase II trial.[1] The study enrolled 265 women with platinum-sensitive relapsed serous ovarian cancer with or without BRCA1 or 2 germline or somatic mutations. Patients must have previously had a complete or partial response to platinum-containing chemotherapy and at least two previous platinum regimens.

Progression-free survival was significantly longer with olaparib compared with placebo (8.4 months vs 4.8 months) but there was no significant difference in overall survival (29.7 months vs 29.9 months).[1] In a subgroup of 136 women with a BRCA mutation, progression-free survival was 11.2 months with olaparib and 4.3 months with placebo.[2] In an analysis of this subgroup, overall survival was 34.9 months in the olaparib arm and 30.2 months in the placebo arm. The difference was not statistically significant.[3]

The most common adverse events with olaparib included nausea (68.4% of patients), fatigue (48.5%), vomiting (31.6%), diarrhoea (22.8%), headache (18.4%), decreased appetite (18.4%), abdominal pain (17.6%), anaemia (16.9%), dyspepsia (16.2%) and dysgeusia (14%). These events were serious (grade 3 or 4) in some patients. Treatment-related events that led to permanent discontinuation with olaparib included palpitations and myalgia, erythematous rash and nausea.[1]

Haematological toxicity was common with olaparib and one patient in the trial died of haemorrhagic stroke associated with thrombocytopenia. Blood counts should be measured before starting treatment and then monthly for the first year of treatment.

Olaparib is genotoxic and should not be used during pregnancy. Taking it during lactation is also not recommended, although it is not known if the drug is excreted in breast milk.

Following oral administration, olaparib is rapidly absorbed and peak plasma concentrations are reached after 1–3 hours. As food slows absorption, capsules should be taken at least an hour after eating and two hours before the next meal. Olaparib is mainly metabolised by cytochrome P450 (CYP) 3A4 so concomitant use of potent CYP3A4 inducers or inhibitors, including grapefruit and Seville oranges, should be avoided.

Olaparib prolonged progression-free survival by 6.9 months in women with BRCA mutant-positive high-grade serous ovarian cancer. Overall survival was also slightly longer with olaparib than with placebo, although this difference was not statistically significant. Patients must have a confirmed BRCA1 or 2 mutation before starting treatment and have already had at least two courses of platinum-containing chemotherapy.

[X] manufacturer did not respond to request for data

REFERENCES

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.