NEW DRUGS

Niraparib

Approved indication: ovarian cancer

Zejula (GlaxoSmithKline)
100 mg capsules

Ovarian cancer often presents late and tends to recur despite chemotherapy. This has led to a search for maintenance treatments for women with recurrent cancer. One approach is to inhibit the enzymes involved in the repair of DNA in tumour cells. In vitro, inhibition of the poly (ADP-ribose) polymerase (PARP) enzymes is cytotoxic and reduces tumour growth. Olaparib is a PARP inhibitor that has been used in ovarian cancer, but its efficacy is in tumours with mutations of the BRCA genes. Niraparib is a PARP inhibitor that may have efficacy in a wider range of tumours.

Patients start treatment within eight weeks of completing a course of chemotherapy. The recommended dose of niraparib is 300 mg once daily. Food does not significantly affect absorption. Most of the dose is metabolised with the metabolites being excreted in urine and faeces. This metabolism does not involve the cytochrome P450 system and there have been no drug–drug interaction studies. The half-life of niraparib is 36 hours, but it is unknown if this and other pharmacokinetic parameters are affected by severe kidney disease or moderate–severe hepatic impairment.

An open-label phase II treatment trial enrolled 463 women who had received a median of four chemotherapy regimens for ovarian, fallopian tube or primary peritoneal cancer. Most of these relapsed cancers had become resistant or refractory to platinum therapy. The patients took niraparib 300 mg daily with a median follow-up of 12.2 months. There was a response to treatment in 8% (38/456) of the women. The response rates varied with the genetics of the tumours. Overall survival was 17.2 months, but it was 26 months if there was a BRCA mutation.[1]

The phase III NOVA trial of maintenance therapy enrolled 553 women with cancer of the ovary, fallopian tube or peritoneum. Despite sensitivity to platinum-based chemotherapy, the cancer had progressed. A BRCA mutation was present in 203 women. The patients were randomised in a 2:1 ratio to daily niraparib or a placebo and followed up for a median of 16.9 months. In the women who had BRCA mutations, the median progression-free survival was 21 months with niraparib and 5.5 months with placebo. The corresponding figures were 9.3 months and 3.9 months for the 350 women without a mutation.

The actions of niraparib are not confined to cancer cells so all patients will experience adverse effects. In the NOVA trial 14.7% of patients given niraparib had to stop treatment because of adverse effects compared with 2.2% of the placebo group.[2] As niraparib suppresses bone marrow, patients are at risk of anaemia, thrombocytopenia and neutropenia. These adverse effects may require treatment to be reduced or stopped, so the blood count should be regularly checked. In the NOVA trial 1.4% of the women taking niraparib developed myelodysplastic syndrome. Regular monitoring should also include pulse and blood pressure. Severe hypertension, including hypertensive crisis, affected 8.2% of the patients in the NOVA trial compared with 2.2% of the placebo group. Other adverse effects that are more frequent with niraparib than placebo include nausea, vomiting, constipation, fatigue, dyspnoea, mucositis and insomnia. Despite these common problems, the NOVA trial reported that the quality of life was similar for patients given niraparib or placebo.[3]

On the evidence to date, niraparib has been approved as maintenance therapy for women with platinum-sensitive, relapsed high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who have had a complete or partial response to platinum-based chemotherapy. However, it is currently uncertain if the advantage of niraparib over placebo in progression-free survival will lead to a confirmed improvement in overall survival. When the NOVA trial was published, 16.1% of patients given niraparib had died compared with 19.3% of the placebo group.[2] Further research will be needed to identify which women are most likely to benefit from a PARP inhibitor. A phase II trial has reported that progression-free survival is greater if niraparib treatment is combined with bevacizumab, compared to niraparib alone (median 11.9 vs 5.5 months).[3] Niraparib maintenance therapy has also been found to improve progression-free survival compared to placebo (median 13.8 vs 8.2 months) in a phase III trial involving women with newly diagnosed advanced ovarian cancer.[4]

[X] manufacturer did not respond to request for data

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2. Mirza MR, Monk BJ, Herrstedt J, Mahner OS, Redondo A, Fabbro M, et al; ENGOT-OV16/NOVA Investigators. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. N Engl J Med 2016;375:2154-64. https://doi.org/10.1056/NEJMoa1611310

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Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

NEW DRUGS

3. Mirza MR, Åvall Lundqvist E, Birrer MJ, dePont Christensen R, Nyvang GB, Malander S, et al; AVANOVA investigators. Niraparib plus bevacizumab versus niraparib alone for platinum-sensitive recurrent ovarian cancer (NSGO-AVANOVA2/ENGOT-ov24): a randomised, phase 2, superiority trial. Lancet Oncol 2019;20:1409-19. https://doi.org/10.1016/S1470-2045(19)30515-7
4. González-Martín A, Pothuri B, Vergote I, DePont Christensen R, Graybill W, Mirza MR, et al; PRIMA/ENGOT-OV26/GOG-3012 Investigators. Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 2019;381:2391-402. https://doi.org/10.1056/NEJMoa1910962

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, and the European Medicines Agency.