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## Olaparib Desensitization in a Patient with Recurrent Peritoneal Cancer

**TO THE EDITOR:** Olaparib, a poly(adenosine diphosphate [ADP]–ribose) polymerase (PARP) inhibitor, is a recommended and effective treatment option for patients who have relapsed, platinum-sensitive ovarian cancer, tubal cancer, or primary peritoneal cancer, regardless of *BRCA* mutation status.<sup>1</sup> Allergic reactions to olaparib have been reported in several patients worldwide. Urticaria developed in 10 of those patients, with one case being classified as severe.<sup>2-4</sup> In patients with drug allergy, desensitization can reduce or eliminate the allergic response to the drug and facilitate the

continuation of a specific treatment. Owing to a paucity of information regarding desensitization to olaparib, we developed a desensitization protocol for the drug.

A 49-year-old woman presented with a platinum-sensitive relapse of a high-grade serous peritoneal cancer with extensive peritoneal and pleural carcinomatosis and effusions. Testing for a germline *BRCA1* mutation was positive. No second somatic mutation was found. The patient had a complete remission after the most recent platinum-based chemotherapy and then began receiving maintenance therapy with olaparib capsules at a dose of 400 mg twice daily. After the patient received the first dose, an allergic reaction developed that was characterized by angioedema and cutaneous wheals. This allergic reaction developed reproducibly within approximately 3 hours after each administration of olaparib and lasted for several hours. Three rechallenge attempts with preventive applications of clemastine (a first-generation H<sub>1</sub>-antihistamine) or bilastine (a second-generation H<sub>1</sub>-antihistamine), with or without the administration of omalizumab (a recombinant, humanized, monoclonal antibody against anti-IgE), were not successful. The patient was assessed and was confirmed to have type I (immediate or anaphylactic) hypersensitivity to olaparib on skin-prick testing. To allow the continuation of olaparib treatment, we used a 2-day desensitization protocol that involved subsequent oral applications of incremental doses of specifically prepared olaparib capsules, with a starting dose of 12.5 mg and a final dose of 800 mg (Table 1). During the desensitization phase, no additional drugs (antihistamines, glucocorticoids, or leuko-

**Table 1.** Olaparib Desensitization Protocol.

| Dose Day and No. | Daily Duration of Protocol | Interval since Previous Dose | Olaparib Dose |                       |
|------------------|----------------------------|------------------------------|---------------|-----------------------|
|                  |                            |                              | Single Dose   | Cumulative Daily Dose |
|                  | hr:min                     | min                          | mg            |                       |
| <b>Day 1</b>     |                            |                              |               |                       |
| 1                | 00:00                      | —                            | 12.5          | 12.5                  |
| 2                | 00:30                      | 30                           | 25            | 37.5                  |
| 3                | 01:30                      | 60                           | 50            | 87.5                  |
| 4                | 02:30                      | 60                           | 100           | 187.5                 |
| 5                | 03:30                      | 60                           | 200           | 387.5                 |
| 6                | 05:30                      | 120                          | 200           | 587.5                 |
| 7                | 08:30                      | 180                          | 300           | 887.5                 |
| <b>Day 2</b>     |                            |                              |               |                       |
| 1                | 00:00                      | —                            | 200           | 200                   |
| 2                | 01:00                      | 60                           | 200           | 400                   |
| 3                | 07:00                      | 360                          | 400           | 800                   |

triene blockers) were used. No adverse reactions were observed during the desensitization.

Mild and transient urticaria and itching developed at the end of the first day. Treatment with the standard dose of olaparib (400 mg twice daily, administered as capsules) on day 2 of the desensitization protocol elicited no hypersensitivity symptoms. Currently, our patient continues to receive olaparib capsules at a dose of 400 mg twice daily, without interruptions, and has had no further signs or symptoms of drug hypersensitivity. Over the 16-month period after desensitization, our patient has continued to have a complete remission. Given the efficacy of olaparib for the treatment of patients with cancer, desensitization can be suggested in patients in whom type I hypersensitivity to this drug develops.

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## Nivolumab and Ipilimumab in Melanoma Metastatic to the Brain

**TO THE EDITOR:** Given the historically poor prognosis associated with brain metastases in patients with melanoma, better therapeutic options are needed. Can Tawbi et al. (Aug. 23 issue)<sup>1</sup> address the following methodologic and logistic considerations pertaining to their study? Considering that 22% of the patients had died at the time of the analysis, could accounting for the competing risk of death have altered the results? Adverse events of grade 3 or 4 were noted in 55% of the patients, and one patient died from immune-related myocarditis. Although most of these adverse events were reversible, managing them inevitably affects patient safety, quality of life, and medical costs.

The experience of one of us (a radiation oncologist) and the literature suggest that stereotactic radiosurgery is safe and effective for the treatment of lesions of the sizes of those in patients enrolled in this study, with minimal to no side effects, even when combined with single-

agent immunotherapy.<sup>2</sup> Can the authors expand on their rationale to initiate immunotherapy without first starting with stereotactic radiosurgery? Given the considerable financial ramifications associated with their strategy, do the authors think the data are mature enough to replace the existing standard of care, which includes stereotactic radiosurgery?<sup>3,4</sup>

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