

What do elderly patients prefer ?

A prospective multicenter study of preference for oral or intravenous treosulfan in elderly patients with recurrent ovarian cancer

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Background and aims:

Treosulfan, an alkylating agent, has demonstrated activity in recurrent ovarian carcinoma. It is effective as oral (PO, 97% bioavailability) and intravenous (IV) formulation. Primary aim of this study is to explore the preference and compliance of elderly patients (age 65 and above) for PO or IV-treosulfan for the treatment of relapsed ovarian carcinoma. Secondary aims are to evaluate geriatric assessment, toxicity, response and survival.

Methods:

Patients had a free choice of treosulfan-IV (7000mg/sq day 1 of a 28-day cycle) or PO (600mg/sq day 1-28 of a 56-day cycle) until disease-progression. Indecisive patients were randomized.

Compliance was measured by patient-requested therapy-discontinuation. A planned interim safety-analysis was performed after 25 of 100 patients.

Results:

25 of 51 recruited patients completed therapy at the time of the interim analysis (median age 75 years, range 70-82). 20 (87% , 95% CI: 66.4 - 97.2%) chose IV and 3 chose PO (p=0.00003, figure 1), 2 were randomized to IV. Median ECOG was 1 (range 0-2), detailed patient characteristics are listed in table 1.

The most frequent concomitant disorders were cardiovascular, musculoskeletal and gastrointestinal problems. A median number of 2 prior chemotherapy-regimens had been applied (range 1-6, table 2). Patients with preference for IV stated that they already took a large number of tablets for concomitant morbidities, were afraid of gastrointestinal toxicity and that their daily life was less affected by monthly infusions.

A median number of 3 (range 1-10) cycles of treosulfan was administered per patient. Hematologic and non hematologic toxicities were generally low, details are listed in tables 3 and 4. The most frequent therapy modification was interval prolongation, the main reason for therapy discontinuation was progressive disease (tables 5 and 6).

Conclusions:

- 42 of 51 patients (20 of 23 with completed therapy) preferred IV-treosulfan
- Toxicity was generally low, especially in this heavily pretreated elderly patient population with numerous concomitant diseases
- The clinical outcome seems to be comparable to other palliative chemotherapy-regimens for relapsed ovarian cancer

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| Age, years | |
|---------------------------------|-------|
| Median | 75 |
| Range | 70-82 |
| ECOG | |
| 0 | 2 |
| 1 | 17 |
| 2 | 6 |
| FIGO-Stage at initial diagnosis | |
| II | 3 |
| III | 18 |
| IV | 4 |
| Histology | |
| serous | 17 |
| other | 8 |

Table 1: Baseline patient characteristics; n=25.

| Progression-free interval | |
|------------------------------|----|
| < 6 months | 5 |
| 6-12 months | 9 |
| >12 months | 11 |
| Number of previous therapies | |
| 1 | 5 |
| 2 | 9 |
| 3 | 7 |
| 4 | 2 |
| >4 | 2 |
| Previous regimens | |
| platinum based | 36 |
| anthracyclin | 6 |
| topotecan | 6 |
| others | 6 |

Table 2: previous therapies; n=25.

| Nonhemat. tox. | Grade 1/2 | Grade 3/4 |
|----------------|-----------|-----------|
| Diarrhea | 2 | 1 |
| Constipation | 11 | 2 |
| Nausea | 16 | 1 |
| Vomiting | 12 | 1 |
| Alopecia | 5 | 0 |

Table 3: Nonhematologic toxicities; n=25.

| Hematologic tox. | Grade 1/2 | Grade 3/4 |
|-------------------|-----------|-----------|
| Neutropenia | 1 | 2 |
| Neutropenic fever | 0 | 0 |
| Thrombopenia | 11 | 1 |
| Anemia | 17 | 1 |

Table 4: Hematologic toxicities; n=25.

| Dose modifications (courses) | |
|----------------------------------|----|
| dose reduction | 4 |
| Schedule modifications (courses) | |
| interval prolongation | 30 |

Table 5: Therapy modifications; n=118 courses

| Reasons for therapy discontinuation | |
|-------------------------------------|----|
| progression | 12 |
| patients request | 3 |
| death | 2 |
| hematologic toxicity | 2 |
| concomitant disease | 1 |
| non hematologic toxicity | 1 |
| others | 1 |

Table 6: Therapy discontinuation

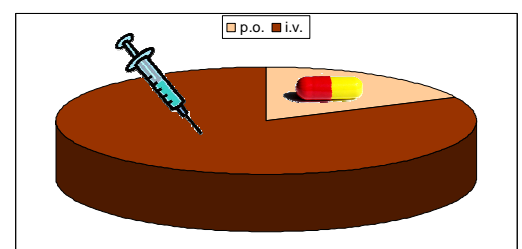


Figure 1: Patient preference regarding oral or i.v. therapy