Chemotherapy-Induced Acute Emesis
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Objectives

1. The second Perugia Consensus Conference took place at the end of March 2004.
2. In patients receiving cisplatin-based chemotherapy, the recommended antiemetic prophylaxis is a single dose of a 5-HT₃ receptor antagonist plus dexamethasone plus the neurokinin₁ receptor antagonist, aprepitant.
3. In patients receiving moderately emetogenic chemotherapy (MEC) the recommended antiemetic prophylaxis is still the combination of a 5-HT₃ receptor antagonist and a corticosteroid.

The first Perugia Consensus Conference took place in 1997 and was organized by the Multinational Association of Supportive Care in Cancer (MASCC). Experts presented on selected topics, which were afterwards discussed among the approximately 300 participants in the meeting. Final recommendations were elaborated the day after the meeting. An overall review of the recommendations were published in Annals of Oncology [1] and ten detailed reviews of the specific topics, discussed during the conference, were published in the journal of Supportive Care in Cancer in 1998.

The second Perugia Consensus Conference took place at the end of March 2004. Again MASCC organized the event, but this time the consensus panel was constituted by 22 experts representing nine scientific societies/organizations within oncology, such as MASCC, ASCO, ONS and ESMO. Ten groups, covering different topics, were appointed with 4-5 of the 22 panel members participating in each group. The groups prepared draft recommendations, which were circulated among the panelists before the consensus meeting. The recommendations were presented and debated during the meeting, and final recommendations elaborated the day after the meeting. These recommendations will be published in one or more scientific journals. Recommendations concerning chemotherapy-induced acute emesis (defined as emesis within the first 24 hours after initiation of chemotherapy) was presented by two groups reviewing prophylaxis in patients receiving highly emetogenic and moderately emetogenic chemotherapy, respectively. Both groups focused on new results appearing since the last consensus conference in 1997. The consensus statements from the conference will be presented in detail.

Prophylaxis of acute emesis induced by highly emetogenic chemotherapy.
Cisplatin is the drug most frequently investigated, meaning that recommendations are of high evidence in patients receiving combination chemotherapy based on cisplatin. In these patients the doses of the different serotonin (5-HT₃) receptor antagonists, including palonosetron, and of the neurokinin (NK)₁ receptor antagonist, aprepitant, are all well-defined. A recent trial investigated different doses of dexamethasone in patients treated with cisplatin-based chemotherapy, and concluded that the optimal dose and schedule is a single dose of 20 mg [2]. Also single doses (not divided) of 5-HT₃ receptor antagonists and of aprepitant are recommended. This means that the recommended prophylaxis of emesis induced by highly emetogenic, cisplatin-based chemotherapy is a single dose of a 5-HT₃ receptor antagonist plus 20 mg of dexamethasone plus 125 mg of aprepitant. Concerning the use of 5-HT₃ receptor antagonists in this setting, oral and intravenous formulations are considered equally effective and the effect and toxicity of the different agents are comparable. A major concern has been the difficulty of maintaining antiemetic effect during multiple cycles of chemotherapy. In a pooled analysis from two randomized, double-blind phase III trials, the addition of the NK₁ receptor antagonist, aprepitant to the combination of ondansetron plus dexamethasone was able to maintain antiemetic effect through six cycles of cisplatin-based chemotherapy [3].

Prophylaxis of acute emesis induced by moderately emetogenic chemotherapy.
The majority of trials have focused on patients treated with cyclophosphamide and/or anthracycline-based chemotherapy. The recommended antiemetic prophylaxis has been the combination of a 5-HT₃ receptor antagonist and a corticosteroid (dexamethasone in most trials). Since the publication of the first Perugia Consensus guidelines [1], the optimal dose of dexamethasone, in the prophylaxis of acute emesis, has been verified as a single 8 mg dose [4]. Two randomized, double-blind studies have compared the effect of the new 5-HT₃ receptor antagonist, palonosetron, with dolasetron and ondansetron respectively [5, 6]. Both studies were designed as non-inferiority studies and showed that palonosetron was at least as effective as ondansetron and dolasetron. At the time of the consensus meeting, no published studies had investigated the use of adding an NK₁ receptor antagonist to the combination of a 5-HT₃ receptor antagonist plus dexamethasone in patients treated with moderately
emetogenic chemotherapy. Consequently, the recommendation is still to use the combination of a 5-HT₃ receptor antagonist plus a corticosteroid (dexamethasone). Also the effect of prophylaxis during multiple cycles was discussed. The effect of a three-drug combination including a 5-HT₃ receptor antagonist plus a corticosteroid plus a dopamine D₂ receptor antagonist seems to be most effective, but even using this combination, the antiemetic effect declined during multiple cycles of moderately emetogenic chemotherapy [7]. Therefore the results of studies investigating the use of NK₁ receptor antagonists are highly warranted.

References