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NCCN Guidelines Panel: Myeloid Growth Factors version 1.2015

On behalf of Hospital Universitario de Getafe, we respectfully request the NCCN (Myeloid Growth Factors version 1.2015) to review some discrepancies found on such guideline with regards to Examples of Disease Settings and Chemotherapy Regimens according to the risk of febrile neutropenia.

Specific Changes:

After a systematic review, which is going to be published on the next issue of the "European Journal of Clinical Pharmacy", of all scientific literature published in the last 20 years of phase III clinical trials evaluating the use of taxanes in the treatment of breast cancer that we have just conducted we have come to find some discrepancies with the NCCN "Myeloid Growth Factors 1.2015 version" guidelines.

On the MGF-A section, "Examples of Disease Settings and Chemotherapy Regimens with a High Risk for Febrile Neutropenia (20%)", docetaxel combined with trastuzumab has been included based on a phase II trial that included 186 patients[1].

Based on our pooled analyses that included 565 patients from 5 treatment arms from 4 phase III clinical trials[2-5] we concluded the real incidence of febrile neutropenia would be 16.3%, below the 20% threshold necessary for a category 1 recommendation. According to our results it should be classified as an Intermediate Risk.

On the same MGF-A section, dose-dense AC followed by T for adjuvant treatment is also included. Although it seems that dose-dense AC might be associated with a higher risk of febrile neutropenia, the recommendation of giving GCSF support during the paclitaxel administration should be reviewed. The referenced article[6] states that overall incidence of hospitalized patients due to febrile neutropenia was 3% for all the protocol.

On our analysis, four phase III clinical trials[7-10], including 4,567 patients, were evaluated. The incidence of febrile neutropenia was 1.1% and it was only 0.6%, when the results of one arm of treatment evaluating a 225 mg/m^2 schedule were excluded.

On the MGF-A section, "Examples of Disease Settings and Chemotherapy Regimens with an Intermediate Risk for Febrile Neutropenia (10-20%)", docetaxel every 21 days is included based on an article[11] that evaluated three trials, only two of them showing febrile neutropenia incidence results. Only one of the two trials, with only 84 patients had an incidence higher than 10% (13%) while in the other one, with 203 patients the incidence is 9%.

In our analyses we included the incidence of febrile neutropenia from 4,212 patients that received docetaxel in monotherapy every three weeks extracted from 17 phase III clinical trials[10,12-27]. Overall incidence was 10.9% which increases the evidence that supports the recommendation.

Paclitaxel every 21 days (metastatic or relapsed) is also included as an intermediate risk regimen based on a phase II trial[28] with 49 patients who started on a 250 mg/m^2 dose, and only those patients with previous treatment started on the more frequently used 175 mg/m2 schedule. Febrile neutropenia occurred in only four cycles (3.6%) among three patients.

Furthermore, our analyses including 1,379 patients from 7 phase III clinical trials[12,13,29-33] showed that the highest incidence reported was 7 %.

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who might also be co-authors or co-contributors of some of these publications.

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Yours sincerely,

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