Concerns regarding data supporting recent PJP prophylaxis guidelines

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To the Editor:

I read with interest the recent guidelines from the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO) on the primary prophylaxis of infections, with specific comment on the recommendations related to *Pneumocystis jirovecii* (PJP).[1] The authors cite and rely heavily on the data and conclusions of the Cochrane Systematic Overview [2] which seems to be the source of their recommendation for routine prophylaxis in patients with “prolonged CD4 < 200/μL” where their Table 5 states that there is “A-I” level supporting evidence (Good evidence to support a recommendation for use with evidence from ≥ 1 properly randomised, controlled trial; from Table 1). However, looking into the primary report from Green *et al* [2] and a derived review publication from the same authors [3] there is no such randomized controlled trial in the context of CD4+ counts <200/μL in patients with hematologic malignancies ever conducted. In fact, the recommendation appears to be derived from “expert opinion” and extrapolated from the HIV infection context without any specific supporting data for the validity of that assumption. Green *et al* incorrectly cite the paper from Kaplan *et al* [4] to support a recommendation for PJP prophylaxis in the HIV context when CD4+ < 200/μL, despite the original Kaplan paper concluding that “... CD4 cell count <250 ... should be considered as criteria for prophylaxis ...”. [4] Green then states “There are no guidelines for *Pneumocystis* prophylaxis in other immunocompromised hosts. Textbook suggestions include chemoprophylaxis in patients with: (4) persistent CD4 counts of less than 200/μL”.

A major issue is the strength attributed to the recommendation in the apparent absence of any supporting data, especially when it is well established that treatment with the nucleoside analogue drugs such as cladribine (2-CdA) or mechanistically related deoxycoformycin (DCF) regularly lead to prolonged CD4 cytopenia < 200/ μL lasting sometimes beyond 5 years, with no episodes of PJP infection reported in the absence of PJP prophylaxis in long-term follow-up of a cohort of 40 patients treated with 2-CdA (105 person-years of follow-up) [5] and 15 treated with DCF (111 patient years of follow-up). [6]

A major role of guidelines is to critically and objectively evaluate and rank the quality of data supporting clinical decision making, and where relevant guiding data is absent, highlight this deficiency. It is not useful for inappropriate strength to be placed on recommendations in the absence of supporting data.

The author declares that he has no conflict of interest.

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