ANEMIA ASSOCIATED WITH NON-CYTOTOXIC AGENTS (PD-[L]1, PARP AND OTHER TARGETED THERAPIES): A REVIEW OF THE LITERATURE

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INTRODUCTION

In patients with advanced cancer, anemia is frequently observed and it is associated with reduced quality of life (QoL), fatigue, decline in physical functions. Besides, consequences of anemia may include impaired response to cancer treatment and reduced overall survival. Different causes can be responsible for anemia in cancer, like bone marrow suppression, reduced iron intake, increased iron losses or anemia of inflammation. However, other pathways blockade, when targeted therapies are used, can be the reason for reduced Hb levels in such patients.

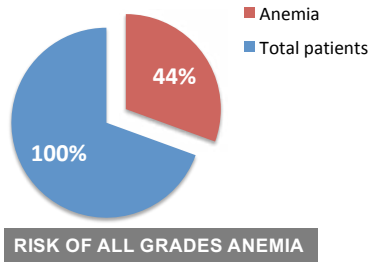
AIM

To study the relation among cancer treatments, mainly non-cytotoxic agents [anti-PD-L1 (programmed cell death-ligand 1), PARP (Poly (ADP-ribose) polymerases)-inhibitors and other targeted therapies], and anemia incidence.

METHODS

Systematic review and meta-analysis, reporting pooled incidence of anemia with biological agents, were considered. We have selected only solid tumors (lung, head and neck, GI, gynecological cancers) and studies regarding hematological diseases were excluded.

RESULTS



Anemia due to immunotherapy was evaluated in a systematic review of 47 studies with PD-(L)1 inhibitors for a total of 9,324 evaluable patients: incidence of all grades G1-4 anemia was 9.8% and G3-4 5% (Fig.1A). Six studies with CDK (cyclin-dependent kinase) 4/6 inhibitors report a risk of all grades and G3-4 anemia of 3.57% and 2.8% (Fig.1B). In PARP-inhibitors, olaparib and niraparib, risk of severe anemia were 8.2 and 25.3% respectively (Fig.1C). The largest effects were associated with avelumab (14.7%), nivolumab (12%) and pembrolizumab (9%) and the lowest with atezolizumab and durvalumab (5.6% and 5%, respectively). Anyway, results for all-grade anaemia were lower with anti-PD-(L)1 compared with conventional agents, with a RR of 0.25.

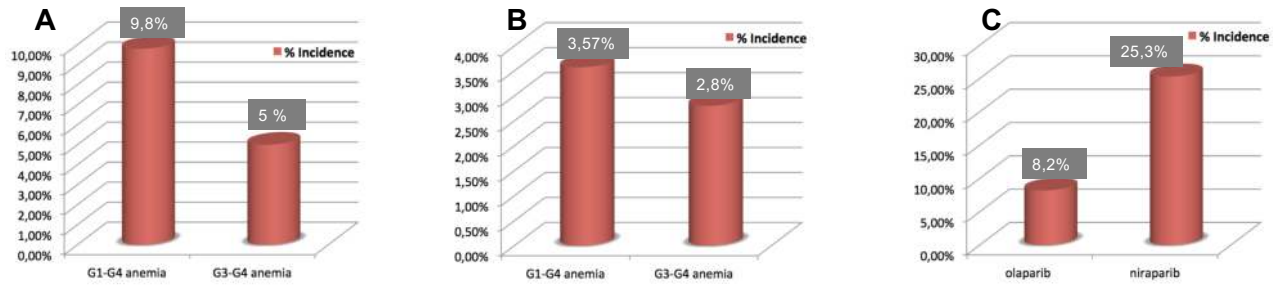
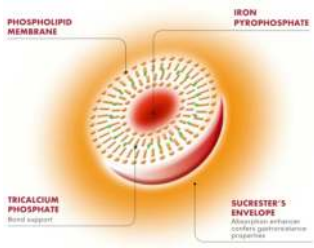


Figure 1 A: Incidence of anemia with PD-(L)1 inhibitors; B: Incidence of anemia with CDK 4/6 inhibitors; C: Incidence of anemia with PARP-inhibitors

CONCLUSIONS

Risk of anemia with targeted therapies is high, about 40-50%, with reduced risk associated with immunotherapy (about 10%). Anemia management is mainly conservative, with supportive care and iron supplementation suggested for mild anemia. Oral iron should be firstly considered, in particular new generation delivery systems, like Sucrosomial® iron that is able to ensure, as per our previous experience, high gastrointestinal tolerability and bioavailability.



Sucrosomial® iron is an oral formulation in which iron is covered by phospholipids plus sucrose esters of fatty acids matrix, allowing a higher iron absorption and bioavailability and avoiding typical gastrointestinal side effects.

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