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POSTER ABSTRACTS

322.DISORDERS OF COAGULATION OR FIBRINOLYSIS: CLINICAL AND EPIDEMIOLOGICAL

Efficacy and Safety of Dapsone in Primary Immune Thrombocytopenia. Results of a Randomized, Placebo-Controlled Multicenter Trial and of a Single-Arm, Emulated Trial in the Prospective, Multicenter Carmen-France Registry

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Introduction:
Adults treated for immune thrombocytopenia (ITP) usually respond to 1 st-line therapy but the majority of them eventually relapse and need a second-line treatment to spare corticosteroids. Dapsone is an antibiotic drug with immunomodulatory properties that has shown some efficacy in various autoimmune diseases including ITP in several retrospective studies. The aim of this study was to assess the efficacy and the safety of dapsone given as second-line for primary ITP.

Methods
DAPS-ITP was a prospective multicenter randomized open-label controlled trial aimed to assess the efficacy and safety of dapsone as a second-line option in adult ITP. Adult patients with primary and newly diagnosed or persistent ITP with previous transient response to corticosteroids and/or IVIg and a platelet count $\leq 30x10^9$/L (or $<50x10^9$/L with bleeding manifestations) were eligible. After randomization (1/1 ratio), patients received either dapsone at 100 mg/day in combination with prednisone for 3 weeks (arm A) or just the 3 weeks course of prednisone (arm B). The primary outcome was the overall response rate (R + CR) in intention to treat at week 52 in the absence of any rescue therapy after week 6 and/or any other treatment for ITP over the study period. Complete response (CR) was defined by a platelet count $>100x\ 10^9$/L on dapsone (arm A) or off treatment (arm B) and response (R) by a platelet count $>30x10^9$/L with a least a doubling of the baseline count.
We also conducted a single-arm, emulated trial in the prospective, multicenter CARMEN-France registry to provide real world evidence about the efficacy and the safety of dapsone in ITP. The CARMEN-France is a prospective, multicenter registry of adult patients with a new diagnosis of ITP in France. We selected the patients included in the registry between 2013 and 2022

with a primary ITP, exposed to dapsone, who met the inclusion criteria of the DAPS-ITP trial. We assessed the same outcomes than in the DAPS-ITP trial.

Results

In total, 93 patients (51% of females, median age 51 years [range: 33-66]) were included and randomized (46 in arm A and 47 in arm B) in DAPS-ITP trial. Median platelet count at inclusion was 25x 10^9/L [17-36], median ITP duration was 0.31 years [0.18-0.90]. Forty-two (arm A) and 45 patients (arm B) were followed up to week 52. In intention to treat (see figure), the overall response-rate (ORR) was respectively 8.70% [2.78%-18.93%] (arm A) and 4.26% [0.78%-12.81%] (arm B) at week 52 (primary outcome, p value = 0.78)). At week 24, the ORR was 25% [11.06%-41.78%] in arm A and 12.77% [5.18%-23.89%] in arm B (p value = 0.57). One death (intracranial hemorrhage) occurred in arm A, none in arm B; 36/46 patients (78%) from arm A had to discontinue prematurely dapsone, mostly for inefficacy with the need of other ITP treatment (n =10/36, 27.7%) or for various safety issues (n=26/36, 72%) including anemia ± gastro-intestinal manifestations (n=6); high methemoglobinemia (n=4); toxidermia (n=3) and others miscellaneous causes (n =13).

In the CARMEN registry, 127 patients were exposed to dapsone. Among them, 50 met the inclusion criteria of the DAPS-ITP trial and had a 52-week follow-up after the initiation of dapsone. Patients characteristics were similar to those included in the DAPS-ITP trial. Three patients had no platelet count measured at W52 ± 4 weeks and were withdrawn from the primary outcome assessment. Overall, 5/47 achieved R or CR at W52 without any concomitant ITP treatment, resulting in an ORR of 10.6%; 95% CI: 3.5-23.1. At W24, 9/45 patients achieved R or CR (ORR: 20.0%; 95% CI: 9.6 -34.6; 5 patients had no platelet count at W24 ± 4 weeks in the real world). Seventeen (34.0%) experienced 19 adverse drug reactions (ADRs) including 8 hemolytic anemia, 4 methemoglobinemia and 3 cutaneous rash. Twelve patients discontinued dapsone due to an ADR.

Conclusion

Among adult patients with primary ITP and a platelet count <30 x 10^9/L treated with dapsone as a second-line treatment, only a minority of patients achieved a sustained response at W52. The low rate of durable response may be at least in part due to an unexpectedly high rate of early discontinuation observed in the dapsone arm (DAPS-ITP trial) due to the occurrence of ADRs, some of which could have been easily manageable outside a clinical trial. Further studies are needed to better define who are the few patients who may still benefit from dapsone, in a cost-effectiveness perspective.

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OffLabel Disclosure: daspone is an old antibiotic with immunomodulatory properties that is used in some autoimmune diseases including ITP based on retrospective studies

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