

# Association between treatment type and therapeutic response according to clinical form of SAPHO syndrome in adults from a multicentre retrospective cohort study

Sirs,

The therapeutic strategy in SAPHO (Synovitis, Acne, Palmoplantar Pustulosis, Hyper-ostosis and Osteitis) syndrome is poorly defined (1). The first-line treatment remains non-steroidal-anti-inflammatory drugs (NSAIDs), which are effective in treating flare-ups but quickly become insufficient (2). Antibiotics have been tried with discordant effectiveness (3). The same applies to conventional immunosuppressive drugs, cs-disease modifying anti-rheumatic drugs. Tumour necrosis factor- $\alpha$  blockers are reserved for refractory forms and their efficacy is uncertain (4). Bisphosphonates (BPs) have shown promise (5).

We conducted a retrospective multicentric study of SAPHO syndrome refractory to NSAIDs over the period 2010 to 2020 to investigate the treatment response degree with BPs or DMARDs according to the radio-clinical picture (predominant bone or predominant joint/mixed). Imaging data made at diagnosis time were reviewed by a radiologist specialised in osteoarticular medicine, blinded to clinical data and treatment received by the patient, to categorise whether the involvement is predominantly

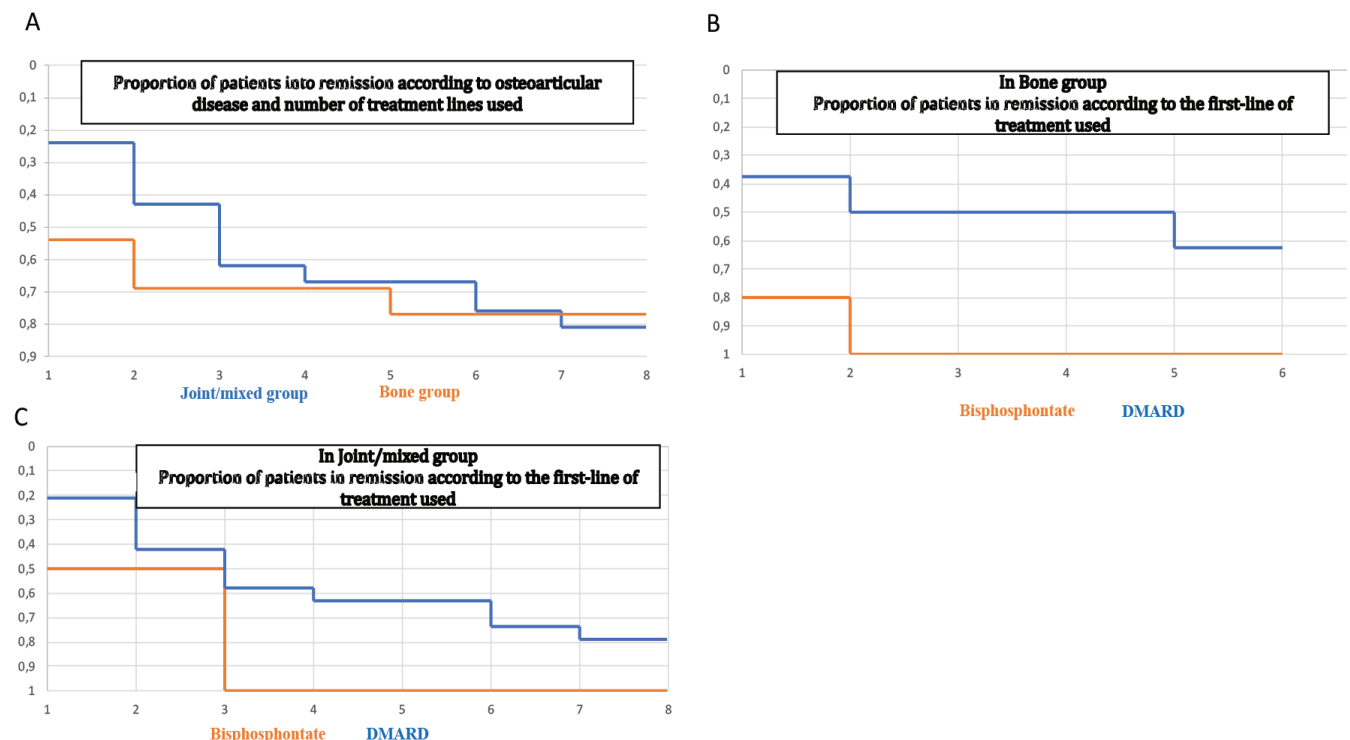
bone or joint/mixed. To carry out a relevant statistical analysis, we grouped together all immunosuppressive drugs to create two groups of specific treatments based either on DMARDs or on BPs. The response to treatment was defined qualitatively according to 2 modalities: efficacy or failure. Treatment efficacy was defined as an improvement in osteoarticular symptoms of at least 50% (cut-off accepted in the literature) (6), with therapy maintenance without escape during follow-up.

Thirty-four patients were included, 21 patients in the joint/mixed group and 13 patients in the bone group. First-line BPs were prescribed significantly more frequently in the bone group than in the joint/mixed group (5/13 and 2/21 patients, respectively), whereas first line DMARDs were prescribed more frequently in the joint/mixed group (19/21 patients) ( $p=0.043$ ). BPs were more effective in the bone group, whereas DMARDs were more effective in the joint/mixed group ( $p=0.002$ ). The bone group required significantly fewer treatment lines than the joint/mixed group (1 line [1–2] vs. at least 2 lines [1–3.5], respectively) ( $p=0.036$ ). Remission tended to be achieved with fewer treatment lines in the bone group than in the joint group (Fig. 1A). Regardless of the group, the use of BPs as first-line treatment appeared to result in more rapid disease control (Fig. 1B–C).

Our results show a significant difference in prescribers' therapeutic attitudes according to the clinical form of SAPHO syndrome,

with a preference for BP as first-line treatment in the bone group and for DMARDs in the joint/mixed group. Despite a possible indication bias, joint/mixed disease appeared to be more difficult to manage since a greater number of treatment lines was used. However, when a BP was prescribed in this group, fewer treatment lines were necessary to achieve remission (Fig. 1C). Zwaenepoel *et al.* have shown, in a cohort of 21 patients under BP, that the treatment line initiated number was fewer (3 vs. 4 or 5 for the other treatments) (7). This is one of the largest multicentric series on SAPHO that has been focused for the first time on professional practices. Nevertheless, there are many biases inherent to a retrospective study on a rare disease, including missing data, classification of patients in two groups according to different imaging modalities, a limited population size and the cut off of 50% improvement used to define a response to treatment that is highly subjective in a disease with potential intricate fibromyalgia symptoms. Imaging to determine the response would be the best objective method but was not possible to manage in a retrospective study.

To conclude, prescription attitudes in this SAPHO cohort seem to be guided by the dominant radio-clinical rheumatological condition. BPs appeared to be more effective to treat SAPHO syndrome with predominant bone involvement which appeared to be easier to treat than articular or mixed forms.



**Fig. 1.** Proportion of patients in remission in the joint/mixed group and the bone group according to the number of treatment lines used (A). Proportion of patients in remission in the bone group (B), and the joint/mixed group (C) according to the first treatment used (BP or DMARD); BP: bisphosphonates; DMARDs: disease-modifying anti-rheumatic drugs.

# Letters to the Editors

## Acknowledgement

The authors are grateful to Nikki Sabourin-Gibbs, CHU Rouen, for her help in editing the manuscript.

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Competing interests: none declared.

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