

**How should Bing Neel Syndrome be treated?**

Monique Minnema, UMC Utrecht Cancer Center, The Netherlands

Bing Neel syndrome (BNS) is a disease manifestation of Waldenström's macroglobulinemia (WM) that results from infiltration of the central nervous system by malignant lymphoplasmacytic cells. The disease is extremely rare and therefore an expertise group comprising of hematologists, neurologists, immunologists and radiologists, published in 2017 a practical guideline for the diagnosis and management of BNS.<sup>1</sup>

Treatment should be offered to symptomatic patients in whom a definitive diagnosis of BNS has been established. The aim of treatment of BNS is to reverse the clinical symptoms and induce long progression free survival. The clinical response can be monitored by use of serial MRI imaging and/or examination of the cerebrospinal fluid (CSF). In recent retrospective surveys with response data of 44 and 34 BNS patients respectively, the overall response rate was 70% to first line therapy and no differences according to type of treatment could be made.<sup>2,3</sup> Therefore, the choice for type of systemic treatment should be made on an individual basis, considering the patient condition, medical history, preference and experience of the physician.

Chemotherapy regimens commonly used for the treatment for BNS are mainly adapted from treatment schedules used in the treatment of PCNSL. These treatments include high dose methotrexate and high dose cytarabine for several cycles. This may be an appropriate treatment for patients considered fit for intensive therapy. However, also with standard dosed fludarabine, cladribine, and bendamustine responses have been achieved.<sup>4</sup> The use of monotherapy with the BTK inhibitor Ibrutinib has recently gained much interest with the publication of some successful case reports. Ibrutinib can pass the blood brain barrier and has been detected at approximately 2% of the serum level.<sup>5</sup> Therefore, higher dosages (560 mg) than the approved WM dosage of 420 mg might be more effective. BNS is sensitive to radiotherapy but due to neurotoxicity first line use of radiotherapy is not recommended and should be reserved for those patients failing other treatment options.

## IWWM-10 Session 13: Saturday, October 13, 2018, Minnema

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