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- All named persons associated with the study
- Patient identifiers within text, tables, or figures
- By-patient data listings

Anonymized patient data may be made available subject to an approved research proposal submitted. Information which is considered intellectual property or company confidential was also redacted.

1.0 ABSTRACT

Title

Real-world evidence study on brentuximab vedotin retreatment outcomes of cutaneous T-cell lymphoma participants.

Keywords

Real-world evidence; brentuximab vedotin; retreatment; cutaneous T-cell lymphoma participants

Rationale and Background

Brentuximab vedotin (Adcetris®) is approved in the EU for the treatment of adult participants with CD30+ CTCL after at least 1 prior systemic therapy. In the pivotal phase III ALCANZA trial a benefit in effectiveness (objective response rate [ORR], progression-free survival [PFS]) was observed for CTCL participants treated with brentuximab vedotin (BV) compared to physicians' choice (methotrexate or bexarotene), nevertheless CTCL is a chronic disease, and the vast majority of participants experience relapse. With limited alternative systemic treatment options for this chronic disease, many CTCL treating physicians consider re-exposure/re-treatment of their participants with BV. To date, there is no published data showing if retreatment of CTCL participants with BV is effective and safe. There have been CTCL participants retreated with BV due to the lack of alternative therapies. To allow the treating physicians to make an informed decision for the treatment of their participant's, collection and publication of these data was needed.

Research Question and Objectives

In the absence of data from clinical randomized trials, how effective and safe is retreatment with BV in adult CD30+ CTCL participants the real-world setting?

Primary objectives were:

1. To describe the effectiveness of BV re-exposure in CTCL participants (ORR, PFS, TTNT)
2. To describe the safety of BV re-exposure in CTCL participants (rate of neuropathy)

Secondary objectives were:

1. To describe treatment patterns of CTCL participants retreated with BV
    a. co-medications used for lymphoma therapy
    b. dose and interval length of BV administrations
2. Comparison of safety and effectiveness of retreatment compared to original (first) therapy

Study Design

This study was a multi-centre, non-interventional retrospective study.

Setting

This study was conducted in 9 hospitals across Europe. The participating countries were France, Germany and Spain.

Population

Adults with confirmed diagnosis of CD30+ CTCL, who have been treated with BV in two or more different lines of therapy.

Variables

The following variables were abstracted from participants' medical charts, depending on availability:

Participant demographics:

- Age and sex

Clinical characteristics at diagnosis:

- CTCL subtype, date of diagnosis, stage at diagnosis, CD30 expression level

Clinical characteristics prior to first and second treatment with BV:

- CTCL subtype, stage at initiation of treatment, CD30 expression level, skin symptoms

For each treatment with BV:

- treatment start date, treatment end date, number of cycles, cycle duration, BV dose (secondary objective)
- adverse events (especially neuropathy and cytopenias, primary objective 2), and reason for treatment discontinuation
- any concurrent or sequential skin-directed therapy/phototherapy and/or radiotherapy taken as part of the systemic therapy treatment, and other systemic therapies (secondary objective)

Clinical outcomes:

- Response to treatment: skin and global response, assessment date and method, date of progression, date of relapse (primary objective 1)

Vital status:

- Last known vital status, disease stage at last known vital status, date of death, cause of death

Data source

A case report form (CRF) was prepared covering the variables above and investigators collected the data based on their participants' medical charts.

Results

Twenty-six participants from seven sites were included for analysis in this chart review, e.g., 9 participants were from France, 9 from Spain and 8 from Germany. The sample was mostly composed by male participants (18, 69.2%). The mean age at diagnosis was 54.8 years (SD 15.7). A higher ORR was observed in the first BV treatment compared to BV retreatment (88.5% vs 54.2%, respectively) and complete responses observed were also higher after first treatment compared to retreatment (38.5% vs 25%, respectively). Observed PFS was numerically higher in the retreatment (9.8 months vs 8.1 months) and after 24 months, 20% of participants were progression free against 10% in the first treatment. In general, most AEs were reported at a higher incidence during the first BV treatment when compared to the other phases. Neuropathies were a common event in both treatment and retreatment ranging from 5.3% to 52.6% in the first and 6.7% to 26.7% in the retreatment. There were 11/26 (42.3%) reports of Grade 1 peripheral neuropathy (PN) and 3/26 (11.5%) reports of Grade 2 of PN at first BV treatment; and 4/26 (15.4%) reports of Grade 1 PN and 3/26 (11.5%) reports of Grade 2 PN upon BV retreatment. Concomitant to BV CTCL treatment was being received by 11 participants (42.3%) at first treatment and by 7 participants at retreatment (26.9%). Of the twelve participants receiving any type of concomitant CTCL treatment at the same line of therapy , 8 (72.7%) received systemic therapy at first BV treatment and 4 (57.1%) at retreatment. Furthermore, chemotherapy was the most used (8 vs 4 for first and retreatment respectively).

Discussion

The study included a total of 26 participants from 3 European countries (France, Spain and Germany). The primary limitation was the small sample size included in the study but given the rarity of the disease as well as the rarity of the participants who have been retreated with BV this is to be expected; thus, the report is only descriptive. Further to limits include studies with a design of retrospective chart review or real-world evidence generally underreport AEs, selection bias is present as only participants included from specialized centers as well as participants who were classified as retreated with BV were included.

The overall safety is comparable between first BV treatment and BV retreatment. The efficacy results demonstrate promising clinical activity with approximately half the participants reaching either complete response (CR) and partial response (PR) even in those who received BV retreatment. The PFS results exhibit comparable results between first BV and BV retreatment.

The finding of this study suggests that re-exposure to BV is effective and generally well tolerated in terms of safety with no new safety signals observed.

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