Real-Life Use of Talimogene Laherparepvec in Centers in Austria and Switzerland

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Objective

Talimogene Laherparepvec (TVEC), a genetically modified GM-CSF expressing HSV1 Virus that preferentially replicates in tumor cells is approved in Europe for use in melanoma patients with inoperable metastatic lesions in stage IIIM1a. Approval was based on the OPITO study1 which did also include patients with distant metastases and demonstrated a 45% and a CR rate of 16.6%. The aim of this study was to assess the outcome of melanoma patients treated with TVEC in a real life clinical setting outside of clinical studies.

Patients and Methods

A retrospective chart review was conducted in 7 melanoma centres in Austria and 1 centre in Switzerland and anonymized data on disease stage, treatment duration, treatment response by investigator assessment following RECIST 1.1, tolerability as well as data on follow up therapies was collected. Due to the nature of a retrospective study not all data points were available for every patient. A total of 62 patients received TVEC since December of 2016 in the participating centres. Two thirds of the patients had stage IIIA melanomas. Among those with stage IV the majority had M1a disease with only soft tissue or lymph node lesions. Two patients with stage IV M1b and M1d who had complete control of their distant metastases and a locoregional progression were treated in parallel with a PD-1 antibody in one case and in parallel with a BRAF/MEK inhibitor combination in the other. In 3 other cases TVEC was used in combination with a PD-1 inhibitor as first line therapy. Baseline characteristics are presented in Table 1.

Results

Data cut off for this analysis was May 2019, the median follow up was 15.5 months (95% CI 11.7-20.6). The median number of intratumoral injection cycles was 9 (Range 1-56). Response assessment was available for 59 of the 62 patients and showed an ORR of 67.7%, with 50% of patients achieving a complete response. Among the 38 responders was a CR of 62.1% with 50% of patients achieving a complete response. When restricted to those patients with PD in the first line setting (n=25) the CR rate was 40.5%. Table 2 shows the investigator assessed response per stage. TVEC was well tolerated in this real life cohort with only 2 of 62 patients stopping treatment because of side effects. A detailed individual patient information is shown in Table 3. The majority of patients was treated within the approved indication, a minority of patients stopped TVEC due to progression or side effects, but no patient due to treatment related death. A detailed plot showing individual patient information on treatments, treatment duration and time point of response is shown in Figure 3. In this real life cohort treatment with TVEC leads to a high overall and complete response rate which is most likely due to selection of patients most likely to benefit from this treatment. This high response rate is in line with a previous, smaller cohort reported. The majority of responses was durable supporting the idea of induction of a systemic immune-response by TVEC. While the majority of patients was treated within the approved indication, a minority of patients with stage IV M1b disease was also treated with TVEC - mostly in patients with stable systemic disease but locoregional progression - with responses observed in some of those patients. TVEC was well tolerated in this real life cohort with only 2 of 62 patients stopping treatment because of side effects. Although documentation of side effects is usually less stringent outside of a clinical study, those side effects recorded do more likely represent clinically meaningful events. If pretreatment with TVEC can alter the response to a subsequent systemic immunotherapy cannot be answered due to the low number of patients requiring those follow up treatment. In summary this real-life cohort study demonstrates that TVEC is a well-tolerated and very effective intratumoral therapy that can be successfully used in patients with injectable lesions that do not require immediate systemic therapy.

References

1 Andtbacka RHI et al., J Clin Oncol. 2015 Sep 1;33(25):2780-8

Conflicts of Interest:

All authors declare no COI in regard to the work presented.

Table 1: patient Characteristics

Table 2: Investigator assessed response

Table 3: Progression and subsequent therapy

Table 3: Side effects during therapy with TVEC

A detailed graph showing individual patient information on treatments, treatment duration and time point of response is shown in Figure 3. TVEC was well tolerated and only 2 out of 62 patients stopped TVEC because of side effects (Fever and consecutive cardiac decompensation, asymptomatic meningitis-encephalitis). The only side effect observed in more than 10% of the patients was fever and chills (Table 4).