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CDRB436BJP01 Study Results Abstract for Public Disclosure

Title

A non-interventional and retrospective study describing the patient profile and treatment patterns in real-world melanoma patients prescribed with Dab+Tram or Enco+Bini in Japan

Keywords

Melanoma, dabrafendib+trametinib (Dab+Tram), encorafenib+binimetinib (Enco+Bini), patient profile, treatment patterns

Rationale and background

The annual incidence of malignant melanoma in Japan and corresponding mortality rate is increasing over the years in parallel of the aging population.

There are multiple treatment options for unresectable melanoma including intralesional therapy, chemotherapy, palliative care, immunotherapy and targeted therapy of signal transduction inhibitors especially for patients with certain gene mutation. Four genomic subgroups of melanoma identified are BRAF, NRAS, NF1, and triple wild-type. In Japan, the overall detection rate of BRAF mutation is approximately 30% - 42% which is the highest as compared to other mutations.

The activated BRAF-mutated kinase can be inhibited by BRAF inhibitors such as vemurafenib, dabrafenib (Dab) and encorafenib (Enco) that attack the BRAF protein directly. Combined use of BRAF inhibitor and MEK inhibitor such as trametinib (Tram), cobimetinib and binimetinib (Bini) can also help to treat BRAF mutated melanoma. Combinations approved in Japan are Dab+Tram in the Year 2016 and Enco+Bini in the Year 2019.

A thorough understanding of the profiles of melanoma patients initiated with either Dab+Tram or Enco+Bini is warranted to understand the differentiation between both treatment cohorts and decisions on selecting drugs for targeted therapy. Other than that, there is also a missing gap on the patient's journey prior to the initiation of combined BRAF inhibitor and MEK inhibitor which might provide insights on the local treatment strategy practice in Japan.

Research question and objectives

The primary objective was to describe demographics and clinical characteristics of Cohort non-adjuvant Dab+Tram and Cohort Enco+Bini by line of treatment (LoT) and Cohort adjuvant Dab+Tram separately.

Secondary objectives were:

- To describe baseline demographics, clinical characteristics and hospital profiles of Cohort adjuvant Dab+Tram, Cohort non-adjuvant Dab+Tram, Cohort Enco+Bini, and the overall cohort separately, at the date of melanoma diagnosis (index date A).
- To describe the treatment patterns after date of diagnosis from 1st LoT until the last LoT available for Cohort adjuvant Dab+Tram, Cohort non-adjuvant Dab+Tram, Cohort Enco+Bini, and the overall cohort separately.
- To describe the discontinuation rate of Dab+Tram or Enco+Bini in Cohort non-adjuvant Dab+Tram and Cohort Enco+Bini respectively by LoT and the discontinuation rate of Dab+Tram in Cohort adjuvant Dab+Tram.

Study design

This study was a non-interventional, retrospective longitudinal study in Japan to describe the patient profile and treatment patterns of adult melanoma patients that were treated with either Dab+Tram or Enco+Bini.

Setting

The study period was from 01 July 2011 to 31 May 2022.

The identification period was from 01 January 2012 to 30 November 2021.

Index date A was the first date of a confirmed diagnosis of melanoma recorded during the identification period.

Index date B for the Cohort adjuvant Dab+Tram & Cohort non-adjuvant Dab+Tram was the first date of a prescription of Dab+Tram recorded at or after index date A.

Index date B for the Cohort Enco+Bini was the first date of a prescription of Enco+Bini recorded at or after index date A.

Subjects and study size, including dropouts

Adult (at least 18 years old) patients with a confirmed diagnosis of melanoma during the identification period, having at least 6 months continuous enrollment and initiated with either Dab+Tram or Enco+Bini were considered.

Overall, 8,745 patients with a diagnosis of melanoma were identified in the database. Of these, 6,978 (79.8%) patients were aged 18 or older and had at least 6 months of enrollment period before melanoma diagnosis. 471 (5.4%) patients were excluded for having a prescription claim with a melanoma treatment recorded within 6 months before the index date A. Of the 6,507 eligible patients, 106 (1.6%) had been prescribed Dab+Tram or Enco+Bini. After exclusion of patients with less than six months of follow-up after tyrosine kinase inhibitor (TKI) initiation and those with other cancers for which the TKIs might have been prescribed, 82 patients remained, distributed between the three cohorts.

The Cohort non-adjuvant Dab+Tram accounted for the majority of patients (N = 67; 81.7%). Most of these patients (N = 55; 82.1%) were prescribed Dab+Tram in the 1st LoT. The Cohort adjuvant Dab+Tram consisted of 7 patients and the Cohort Enco+Bini of 16 patients. In the Cohort Enco+Bini, 4 patients (25.0%) were prescribed Enco+Bini in the 1st LoT.

Variables and data sources

The primary objective involved demographics and clinical characteristics at the time of treatment initiation.

Secondary objectives involved demographics and clinical characteristics at the time of diagnosis; treatment patterns (common treatment regimen, switching and discontinuation of targeted therapy).

Analyses were based on hospital-based claims data.

Statistical methods

All the main analyses were summarized descriptively. Counts and percentages were presented for categorical variables; measures of central tendency (mean and median) together with standard deviations, quartiles (25th and 75th), minimum and maximum were used to summarize the continuous variables. Summaries were presented together with estimates and corresponding 95% confidence intervals as appropriate.

All analyses were conducted using SAS version 9.4 or higher.

Results

Out of 82 patients of the study population, the Cohort non-adjuvant Dab+Tram accounted for the majority of patients (N = 67; 81.7%). Most of these patients (N = 55; 82.1%) were prescribed Dab+Tram in the 1st LoT. The Cohort adjuvant Dab+Tram consisted of 7 patients and the Cohort Enco+Bini of 16 patients. In the Cohort Enco+Bini, 4 patients (25.0%) were prescribed Enco+Bini in the 1st LoT.

Patients from the Cohort adjuvant Dab+Tram and Cohort non-adjuvant Dab+Tram initiated Dab+Tram in 2016 whereas patients from the Cohort Enco+Bini started Enco+Bini in 2019.

There were more males than females (56.1% vs 43.9%) and almost two thirds of patients were treated in hospitals with ≥500 beds. At the melanoma diagnosis, patients were aged on average 61.3 years (± 13.5), the body mass index (BMI) mean value was equal to 23.7kg/m² (±3.6) and the mean Charlson Comorbidity Index (CCI) score was 4.2 (± 3.3). The median time from the diagnosis to the targeted therapy initiation was 3.6 months in the Cohort adjuvant Dab+Tram, between 10.8 and 12.6 months in the Cohort non-adjuvant Dab+Tram and between 10.7 and 39.2 months in the Cohort Enco+Bini. Patients were more severe at the targeted therapy initiation with the median CCI score equal to 3.0 in the Cohort adjuvant Dab+Tram, between 8.0 and 10.0 in the Cohort non-adjuvant Dab+Tram and 10.5 in the Cohort Enco+Bini.

In the Cohort non-adjuvant Dab+Tram combined with the Cohort Enco+Bini, Dab+Tram was the most commonly prescribed treatment in the first three LoTs with 56 patients (73.68%), 15 patients (19.7%) and 7 patients (16.3%) in 1st, 2nd and 3rd LoT, respectively. In the Cohort non-adjuvant Dab+Tram, 18 patients switched from Dab+Tram in the 1st LoT to another therapy in 2nd LoT with a majority switching to nivolumab alone (7 patients). No patient switched from Enco+Bini in the 1st LoT to another therapy in the Cohort Enco+Bini.

Discussion

The study provides a comprehensive overview of demographics and clinical characteristics and real-life treatment patterns in cohorts of adult melanoma patients receiving concomitant treatment with either Dab+Tram or Enco+Bini.

The majority of patients from our study received Dab+Tram (mostly non-adjuvant) whereas Enco+Bini was administered only to a small number of patients. Dab+Tram was usually prescribed in the 1st LoT, whereas Enco+Bini was mainly in the 2nd or 3rd LoT. This difference might be explained by the fact that Dab+Tram was approved before Enco+Bini.

In the Cohort non-adjuvant Dab+Tram combined with the Cohort Enco+Bini, Dab+Tram was the most commonly prescribed treatment in the first three LoTs. The authors of the Japanese Dermatological Association guidelines noted that there was no data available that compared Dab+Tram with other treatment options available in Japan for adjuvant therapy in patients with resected BRAF-mutant melanoma such as nivolumab or pembrolizumab, thus no robust data were available at the time of this study regarding the ideal treatment strategies (Nakamura et al., 2020). However, the European Society for Medical Oncology (ESMO) guidelines recommended immunotherapies upfront in 1st LoT irrespective of the BRAF mutation status, and BRAF/MEK inhibitor combination therapies (Dab+Tram, vemurafenib+cobimetinib and Enco+Bini) for patients who are not suitable for immunotherapies (Sharma et al., 2019).

In the Cohort non-adjuvant Dab+Tram and the Cohort Enco+Bini, molecular target drugs were the most prescribed therapies in 1st, 2nd and 3rd LoTs, followed by immune checkpoint inhibitors. In the 1st LoT, molecular target drugs were prescribed in 80% of patients and 32% of patients switched to another molecular target drug and 21% to immune checkpoint inhibitors in the 2nd LoT.

Regarding demographic and clinical characteristics, patients treated with Enco+Bini were slightly younger at the time of melanoma diagnosis than those treated with Dab+Tram. Women were overrepresented in the Cohort Enco+Bini and men in the Cohort non-adjuvant Dab+Tram. To our knowledge, there are no differences between indications in terms of patients age and gender, but observed differences in treatment groups may result from the small sample size especially in the Cohort Enco+Bini.

A major limitation of this study was the relatively low number of patients (<20) that were included in the adjuvant Dab+Tram and Enco+Bini cohorts. In addition, it was not possible to continuously track information on patient treatments or diseases when a patient had changed providers or procedures took place in different hospitals. Treatments and prescriptions that were issued in other institutions were not captured in the database. Other limitations related to the database study were e.g., study sample, which was not randomly selected, no information was available on why treatments were started, switched or stopped and whether the patient took the medication prescribed, and treatment patterns were based on prescriptions.

The results from this study may not be generalized to the general Japanese population treated for a melanoma with Dab+Tram or Enco+Bini due to the relatively small size of the population especially for the Cohort Enco+Bini.

Conclusion

This study provides information on how dual TKI therapy targeting BRAF and MEK is used for the treatment of melanoma in Japan in the real-world treatment setting. There were no obvious differences between the profiles of patients treated with Dab+Tram or Enco+Bini. The study highlights that Dab+Tram and Enco+Bini are used consistently with clinical practice guidelines in the metastatic setting. It is important for dermatologists in Japan to ensure that these dual TKI therapies are used in an optimal way to prevent progression of this generally fatal type of skin cancer in Japan. This study provides important information on clinical characteristics of patients treated with dual TKIs. However, further studies are needed to explore these characteristics further, including the social context.

References

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