Combi-EU: BRAF-/MEK-Inhibition with Dabrafenib and Trametinib in Melanoma Patients in the Adjuvant Setting: Interim Analysis of an Observational Study on a Treatment supporting Electronic Health App.

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Introduction & Objectives

To improve prognosis in high-risk melanoma patients, adjuvant BRAF-/MEK-Inhibition (BRAF/MEK-i) with dabrafenib and trametinib has been proven efficient in clinical studies with improved overall and relapse free survival. However, with no evident disease and substantial side effects, compliance might be impaired. Combi-EU investigates a potential benefit of patient supportive tools and a health tracking app on therapy adherence in patients with resected stage III melanoma.

Primary endpoint: assessment of time on treatment (TOT) stratified by patients who used the app and those who do not

Secondary endpoints:

- Side effect management
- correlation analysis of TOT vs. quality of life (QoL) and side effects of BRAF/MEK-i with particular emphasis on pyrexia management

Materials & Methods

- Patients (n = 182) with adjuvant combination therapy of dabrafenib/ trametinib after complete surgical resection of stage III BRAF (V600) mutated cutaneous melanoma
- offered to use a supportive health app (CANKADO®) for free
- Side effects (adverse drug reactions; ADR) and quality of life (QoL) are documented during visits with the EORTC QLQ-C30 Questionnaire
- Treatment modifications for side effects are classified as “managed” if following common recommendations
- TOT and rTOT (censored for relapse) are assessed by Kaplan-Meier Analysis

Results

So far, 29 (42 %) of the 69 patients who accepted to register the app have used it actively. For baseline co-variates there is a significantly lower mean age in app users (52 vs. 59 years, p < 0.01, Table 1). Median TOT at data cut is slightly higher in patients using the app, although not statistically significant (Fig.1A, p = 0.06). The same trend can be observed for median rTOT (Fig.1B, p = 0.17).

	Without app (N=153)	With app (N=29)	Overall (N=182)
Gender			
Female	65 (42.5%)	10 (34.5%)	75 (41.2%)
Male	88 (57.5%)	19 (65.5%)	107 (58.8%)
Age			
Mean (SD)	59.3 (14.1)	52.2 (13.1)	58.2 (14.2)
Median [Min, Max]	59.0 [24.0, 87.0]	55.0 [20.0, 71.0]	58.0 [20.0, 87.0]
ECOG			
0	136 (88.9%)	25 (86.2%)	161 (88.5%)
1	10 (6.5%)	3 (10.3%)	13 (7.1%)
2	2 (1.3%)	0 (0%)	2 (1.1%)
Unknown	5 (3.3%)	1 (3.4%)	6 (3.2%)
Stage III			
Primary	123 (80.4%)	24 (82.8%)	147 (80.8%)
Recurrent	30 (19.6%)	5 (17.2%)	35 (19.2%)
AE type			
Patients without pyrexia	115 (75.2%)	20 (69.0%)	135 (74.2%)
Patients with pyrexia	38 (24.8%)	9 (31.0%)	47 (25.8%)
ADR management			
not applicable	59 (38.6%)	10 (34.5%)	69 (37.9%)
managed	47 (30.7%)	12 (41.4%)	59 (32.4%)
not managed	47 (30.7%)	7 (24.1%)	54 (29.7%)

Table 1: Demographics in relation to using an electronic health app

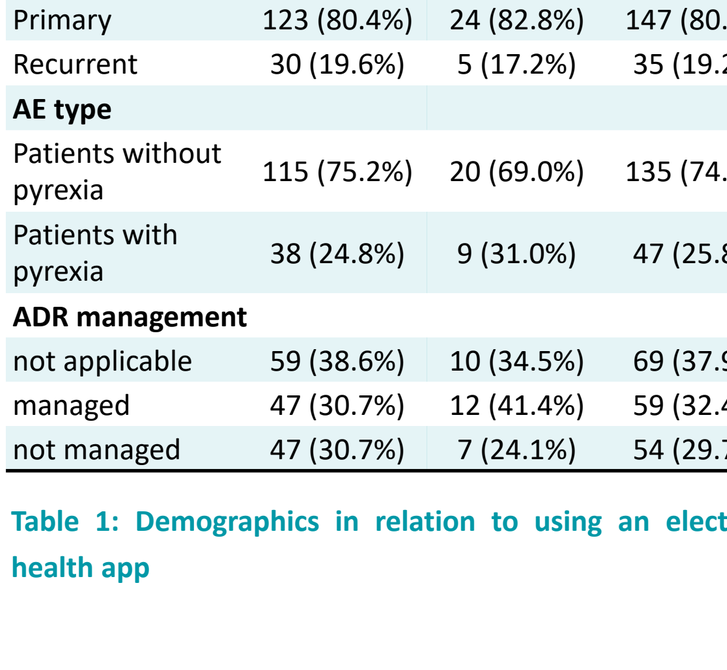

Fig. 1: Interim Time on Treatment for BRAF/MEK-I in relation to using an electronic health app. A) TOT was calculated as time from start of adjuvant treatment until permanent discontinuation of any cause. B) rTOT with censored relapse events. Yellow: app used. Blue: app not used. Statistical differences were assessed by log-rank test.

Adverse events are less impairing TOT and rTOT if treatment modification recommendations are followed (Fig 2). The hazard ratio for premature treatment stop was 0.47 for “managed” treatment modifications versus “unmanaged” ADR handling.

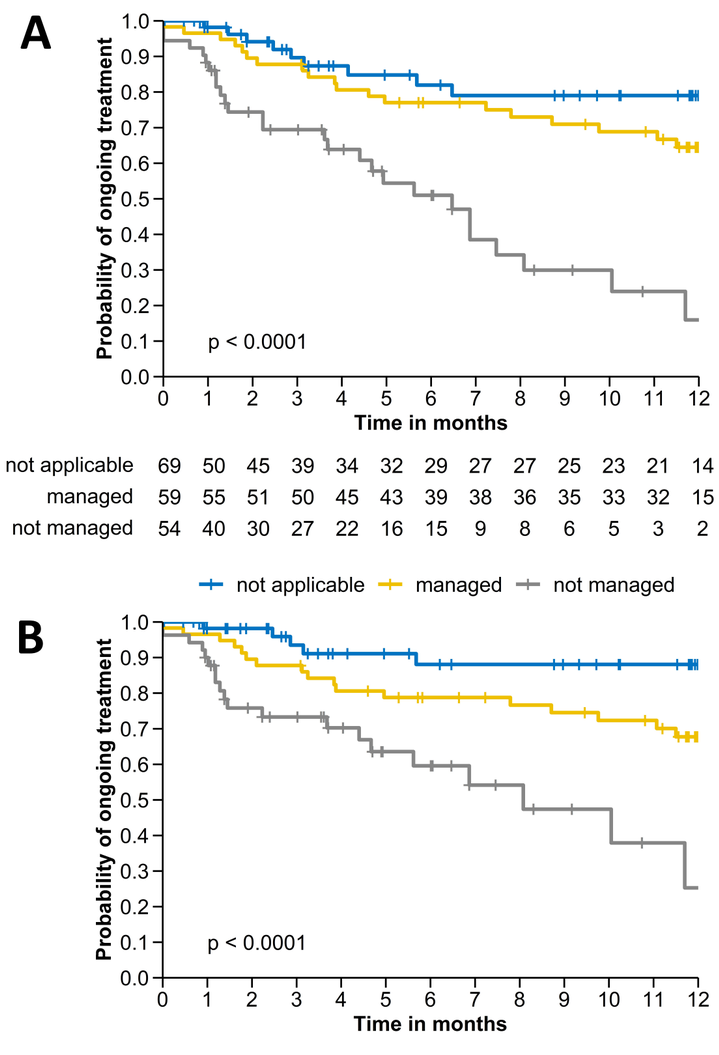

Fig. 2: Interim Time on Treatment for BRAF/MEK-I in relation to side effect management. A) TOT was calculated as time from start of adjuvant treatment until permanent discontinuation of any cause. B) rTOT with censored relapse events Active side effect management (yellow) included dose reductions, pausing, and/or re-challenge. Statistical differences were assessed by log-rank test.

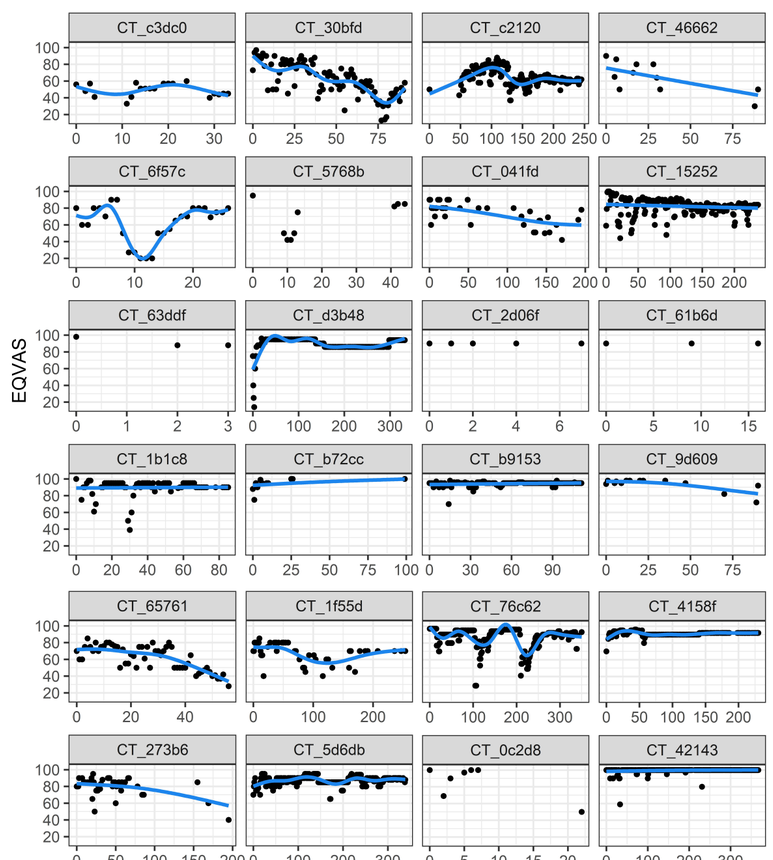

Fig. 3: Global health status (EQVAS) based on duration of app usage for an example of Cankado® app users. User profiles reflect the heterogeneity of therapy experience in patients.

Conclusions

Parameters measuring health related quality of life seem favourable in patients using a supportive electronic app. The correlation between these patient oriented tools and QoL and potentially TOT might indicate better therapy adherence in app users. However, the acceptance rate for using the app is remarkably low limiting the statistical significance of the study results so far and indicating the need for improving electronic health tools by design and particularly for elderly patient populations.

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