Long-term survival follow-up from the REDUCTOR trial: Neoadjuvant cytoreductive treatment with BRAF/MEK inhibition of prior unresectable regionally advanced melanoma to allow complete surgical resection


Background

- Approximately 5% of locally advanced stage III melanoma patients present with unresectable disease, making standard of care with resection followed by adjuvant therapy impossible.1
- 3-year relapse-free survival (RFS) rates for stage III melanoma are 45.0% and 22.2% with adjuvant pembrolizumab or without adjuvant treatment, respectively.2
- The REDUCTOR trial demonstrated that neoadjuvant dabrafenib plus trametinib allowed resections in 18/21 (86%) of patients with prior unresectable locally advanced BRAF-mutated melanoma, including 17 (81%) radical (R0) resections.1
- Major pathologic responses (MPR) were seen in 9/18 patients undergo ing surgery.5
- After a median follow-up of 50 months, recurrences were observed in 50% of patients.5
- Here, we present an update of long-term RFS, progression-free survival (PFS) and overall survival (OS).

Methods

- The single-arm phase II REDUCTOR trial included patients with unresectable, BRAF-mutated, locally advanced stage IIIC or oligometastatic stage IV melanoma.
- 21 patients were treated with neoadjuvant dabrafenib plus trametinib for 8 weeks.

Study design REDUCTOR trial

- PET/CT and physical examination were performed to evaluate response.
- If sufficient downsizing of the tumor was observed, surgical resection was performed.
- Adjuvant therapy was not routinely given.
- The primary endpoint was the percentage of patients achieving a R0 resection.
- Secondary endpoints were RFS, PFS and OS.

References


Survival outcomes according to pathologic response

At a median follow-up of 80.9 months (IQR 38.6-89.7 months), the median RFS in patients that underwent surgery was 15.4 months (95% CI 8.89-not reached). The median PFS in all patients was 12.4 months (95% CI 8.68-not reached). Recurrences were seen in 10/18 patients undergoing surgery, most of which occurred in the first year after resection (8/10). One patient recurred after 1 year and one after 5 years.

The median OS was not reached. The 1-year, 3-year and 5-year OS were 100%, 85% (95% CI 70.7-100.0), 75% (95% CI 58.2-96.6), respectively.

Survival outcomes

- RFS Median 15.4 months (95% CI 8.89-not reached)
- PFS Median 12.4 months (95% CI 8.68-not reached)
- OS Median not reached

Recurrences per pathologic response

- Survival outcomes based on pathologic response (MPR vs non-MPR as illustrated above and PR vs non-PR) did not show significant differences.
- In total, 1/6 patients (17%) with a pathologic complete response (pCR) developed recurrence, compared to 4/5 patients (80%) with a pathologic non-response (pNR).
- Late recurrences (after >1 year) were seen in a patient with a near-pCR and a patient with a pNR.

Conclusions

The primary endpoint was the percentage of patients achieving a Major pathologic responses (MPR) were seen in 9/18 patients undergoing surgery. After a median follow-up of 50 months, recurrences were observed in 50% of patients. Here, we present an update of long-term RFS, progression-free survival (PFS) and overall survival (OS).

Survival status

- Follow-up after surgery
- Non-recurrence (n=10)
- Recurrence (n=8)
- No response (n=1)

No evidence of disease (NED), death (D), alive with disease (AWD), death of disease (DOO).

Subsequent treatments included surgery (n=5) or BRAF/MEK inhibitors (n=3) as first therapy, immunotherapy (n=2); surgery (n=3), BRAF/MEK inhibitors (n=2) or radiotherapy (n=3) as second therapy. Beyond second-line therapies were given in 8/10 patients and included surgery, immunotherapy, BRAF/MEK inhibitors and radiotherapy.

Author information

The presenting author F.H. Burgers declares no competing interests.

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