Second-line nintedanib + docetaxel for patients with lung adenocarcinoma after first-line immuno-chemotherapy treatment: updated efficacy and safety results from VARGADO Cohort C


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A hypothesised angio-immunogenic switch

Methods

VARGADO (NCT02324858) is a prospective, non-interventional study of nintedanib plus docetaxel in combination with standard 1L CT where the tumour microenvironment (TME) was monitored. To assess the potential of an "angio-immunogenic switch", tumoural immune response, T cells and immunosuppressive cell function were examined. A total of 547 patients from centres across Germany were enrolled in centres across Germany.

Patient cohorts in VARGADO

1L: Nintedanib + CT
2L: Nintedanib + docetaxel
3L: Nintedanib + docetaxel

Results

Patient and disease characteristics (n=137)

- Median age: 63 years (range 37–89)
- Gender: 92 female (43.1%), 45 male (28.5%)
- EGFR mutation status: 33 (28.5%); 44 (38.7%); 28 (23.4%); 8 (6.8%)
- PD-L1 expression: Not reported
- Brain metastases present: 27 (19.7%)
- ECOG PS: 39 (28.5%)
- Best response (n=80 evaluable patients)
  - Complete response: 1 (1.3%)
  - Partial response: 32 (40.0%)
  - Stable disease: 43 (53.8%)
  - Progressive disease: 22 (27.5%)

Efficacy outcomes

- Overall survival (median PFS: 4.8 months; ORR: 37.5%, DCR: 72.5%)
- Progression after 1L CT and subsequent ICI therapy

Safety and tolerability

- TEAEs by drug relationship in the treated set (n=137)
  - Diarrhoea: 42 (31.0%)
  - Decreased appetite: 5 (5.0%)
  - Fatigue: 40 (29.2%)
  - Nausea: 39 (28.5%)
  - Vomiting: 37 (27.0%)
  - Myalgia: 34 (25.0%)
  - Pyrexia: 13 (9.5%)
  - Headache: 11 (8.0%)
  - ALT/AST: 1 (0.7%)

Key findings and conclusions

Second-line nintedanib plus docetaxel has clinically meaningful efficacy following failure of 1L ICI (median PFS: 4.8 months; ORR: 37.5%, DCR: 72.5%).

Nintedanib plus docetaxel showed efficacy regardless of the time since start of 1L treatment (>9 vs 29 months) and KRAS mutation status.

Treatment was tolerable with no unexpected safety signals.

Nintedanib plus docetaxel should be considered as a treatment option in patients with adenocarcinoma following failure of ICI therapy.

Recruitment and follow-up are ongoing for patients in this cohort; updated results will be presented at a later date.

References and acknowledgments


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Results (cont’d)

Responses were observed in both patients with fast-progressing and slower-progressing disease

Overall time on treatment and best responses for PD in patients with >9 months (n=89) and ≥9 months (n=48) since start of first-line therapy

Nintedanib plus docetaxel is well tolerated in routine clinical practice

There were no new safety signals or unexpected toxicities

TEAEs by drug relationship in the treated set (n=137)

Grade 1–2 emetic adverse events; grade 3–4 neutropenia

Sustained tolerability of CT was observed in long-term follow-up

Grade 33 TEAEs/treatment-related TEAEs were observed in 45.3%/36.5% of patients

Nintedanib dose reductions and therapy interruptions were reported in 33.6% and 21.9% of patients, respectively

Dose reductions and therapy interruptions were reported in 13.1% and 16.1% of patients, respectively

TEAEs leading to discontinuation were reported in 40 patients (29.2%)

Related TEAEs occurring over time on treatment (CT, +/− ICI) and best responses to treatment plus discontinuation

Clinical outcomes for the full cohort and patients with ≥3 months (n=118) and <3 months (n=19) since start of first-line therapy

PD and control rate (objective response rate) were encouraging

PD in the treated set (n=137)

Nintedanib plus docetaxel showed evidence of the "angio-immunogenic switch" following 1L CT

Centralised review of patients with ≥3 months was performed

There were no unexpected safety signals or events

Nintedanib plus docetaxel is well tolerated in routine clinical practice

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PD in the treated set (n=137)