Outcomes Following Continuation or Stopping Long-Term Mepolizumab Treatment in Patients With Severe Eosinophilic Asthma: The Randomized COMET Trial

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Background

Mepolizumab is a targeted anti-interleukin (IL)-5 monoclonal antibody that has been approved for the treatment of severe eosinophilic asthma and eosinophilic granulomatosis with polyangiitis.[1]

The efficacy and safety of long-term treatment with mepolizumab in patients with severe eosinophilic asthma have been demonstrated for up to 4.5 years in previous double-blinded[2–5] and open-label studies.[6–8]

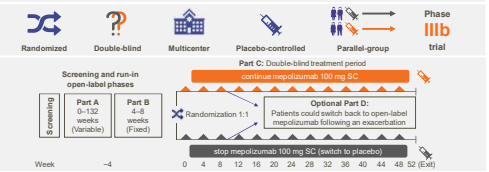
There are no data on the impact of stopping treatment after longer than 1 year of mepolizumab treatment.

The COMET study assessed outcomes in patients with severe eosinophilic asthma who had been treated with mepolizumab 100 mg administered subcutaneously (SC) for ≥3 years and then either stopped or continued long-term treatment.

Methods

Study design

GSK ID: 201810; NCT02555371



Inclusion criteria

- Received continuous mepolizumab treatment **for ≥3 years***
- Completed the previous open-label mepolizumab studies, COLUMBA[1] or COSMEX[2]
- Remained on asthma controller therapy, throughout COLUMBA[1] or COSMEX[2]

Exclusion criteria

- A clinically significant health deterioration at completion of COLUMBA[1] or COSMEX[2]
- <80% adherence to controller medications during COLUMBA[1] or COSMEX[2]
- Current smokers
- Treated with any mAb other than mepolizumab within 5 half-lives of screening

Study endpoints

Primary endpoint
- Time to first clinically significant exacerbation (requiring systemic corticosteroids, ED visit or hospitalization)

Secondary endpoints
- Time to first exacerbation requiring ED visit/hospitalization
- Blood eosinophil count ratio to baseline
- Time to decrease in asthma control (ACQ-5 score increase from baseline ≥0.5-points)

Other endpoints
- Time to first exacerbation requiring hospitalization
- Safety

*With no treatment gaps >12 weeks between any two mepolizumab doses (84 days, equivalent to >2 consecutive missed doses).

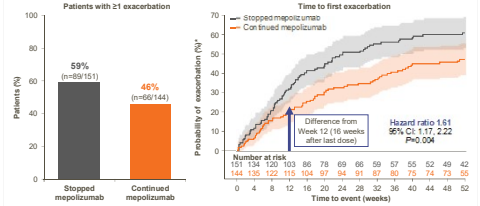
Results

Demographics and disease characteristics at COMET randomization were similar in both groups

	Stopped mepolizumab (N=151)	Continued mepolizumab (N=144)
Female n (%)	86 (57)	87 (60)
Age years, mean (SD)	56 (11.4)	57 (11.5)
Duration of asthma years, mean (SD)	23 (13.8)	25 (14.5)
Exacerbations in previous year mean (SD)	0.6 (1.1)	0.8 (1.5)
ACQ-5 score mean (SD)	1.2 (1.04)	1.4 (1.05)
Using maintenance OCS n (%), Median (range) dose, mg/day*	17 (11) 5.0 (0.0–20.0)	21 (15) 5.0 (0.0–20.0)
Blood eosinophil count cells/μL, geometric mean (SD of log)	40 (0.870)	50 (0.881)

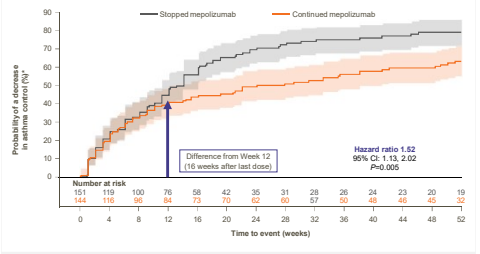
*Prednisone equivalent dose. OCS, oral corticosteroids; SD, standard deviation

Time to first clinically significant exacerbation was significantly shorter for those who stopped versus continued long-term mepolizumab



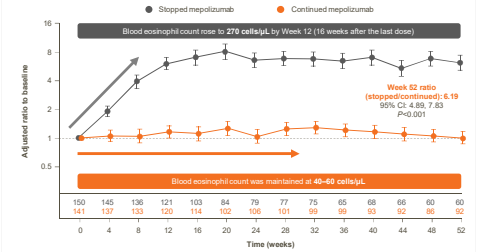
*Kaplan–Meier cumulative incidence curve; shaded areas represent 95% CIs. Hazard ratio estimated using Cox proportional hazards models adjusted for covariates. CI, confidence interval

Patients who stopped mepolizumab treatment had a significantly shorter time to a decrease in asthma control than those who continued



*Kaplan–Meier cumulative incidence curve; shaded areas represent 95% CIs. Hazard ratio estimated using Cox proportional hazards models adjusted for covariates.

Blood eosinophil counts increased in those who stopped mepolizumab versus those who continued; increases were maintained until Week 52



Analyzed using mixed model repeated measures adjusted for covariates.

Conclusions

- Patients with severe eosinophilic asthma who stopped long-term (≥3 years) mepolizumab treatment had the following, versus those who continued:
  - An increase in exacerbations and shorter time to first exacerbation
  - A reduction in asthma control
  - An increase in blood eosinophil counts back to pre-treatment levels[2–4]
  - Differences in efficacy outcomes were seen from Week 12 (16 weeks after the last dose)
  - Data from COMET show a safety profile of mepolizumab consistent with previous trials[2–8]
- These results support continued mepolizumab treatment having sustained clinical benefits in patients with severe eosinophilic asthma

Other key results

- Exposure to mepolizumab was shorter for the 'stopped mepolizumab' group than for the 'continued' group during the treatment period (94 vs 115 patient-years, respectively).
- Exacerbations requiring hospitalization or an ED visit and exacerbations requiring hospitalization were rare in both groups (5% vs 7%, and 4% vs 1%, in the 'stopped' and 'continued' groups, respectively).
- The number of adverse events per 1000 patient-years exposure was similar in both groups (3098 and 2740 in the 'stopped' and 'continued' groups, respectively); the safety profile of mepolizumab was consistent with previous trials.

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The oral presentation slide deck and an accompanying video recording can be accessed by scanning the QR code or via http://tago.ca/ats04

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