Background

Multiple Myeloma (RRMM)

Belantamab mafodotin is a first-in-class, anti-BCMA immunooconjugate with an anucleosided, humanized anti-BCMA mAb conjugated by a protease-resistant maleimidoaryl linker to a micromolar-disrupting agent, monomethyl auristatin F.1

Upon binding to BCMA, belantamab mafodotin is rapidly internalized and the cytotoxic moiety is released, antibody-dependent cellular phagocytosis is mediated, antibody-dependent cellular cytotoxicity is enhanced, and immunogenic cell death occurs.2,10

Belantamab mafodotin (GSK2857916) is an approved therapy for patients with RRMM receiving dexamethasone (pom/dex) who have progressed after 2 prior lines of therapy.7

In the first-in-human Phase 1 study (DREAMM-1/BMA117159, NCT02064387), belantamab mafodotin (3.4 mg/kg QW) monotherapy demonstrated a manageable safety profile and deep and durable clinical responses in patients with RRMM.10

In the larger MM-010 (STRATUS) Phase 3b trial of belantamab mafodotin (3.4 mg/kg QW), monotherapy demonstrated a manageable safety profile and deep and durable clinical responses in patients with RRMM.11

To evaluate the efficacy and safety of single-agent belantamab mafodotin in patients with RRMM receiving pom/dex who have progressed after 2 prior lines of therapy, the DREAMM-3 trial was conducted.

Study design

This study (NCT04162210) is:

- Phase 3
- Open label
- Randomized
- Two-arm
- Multicenter

Ongoing study with patients with RRMM:

- ORR of 60% (95% CI: 42.1, 76.1)
- Median PFS of 12.0 months (95% CI: 9.8, 14.8)
- Median DoR of 14.3 months (95% CI: 10.6, NE)

In a cohort of 35 heavily pretreated patients with RRMM results were:

- ORR of 33% (95% CI: 26.4, 40.6)
- Median PFS of 6.0 months (95% CI: 3.9, 7.1)

Key inclusion criteria:

- Prior BCMA-targeted therapy or pom treatment
- Prior allogeneic SCT
- ECOG PS 0–2
- ≥18 years of age

Key exclusion criteria:

- Active renal condition, unstable liver or biliary disease, active bleeding
- Treatment with an anti-MM monoclonal antibody
- Prior BCMA-targeted therapy or pom treatment
- Prior allogeneic SCT

Exploratory endpoints:

- Baseline BCMA expression, changes in soluble BCMA and circulating free DNA
- Time to best response
- PFS on subsequent line of therapy
- Further evaluation of changes in safety assessments, including vital signs and ECOGs
- Further evaluation of changes in symptoms and HRQoL
- Further PK profiling
- Relationships between belantamab mafodotin exposure and efficacy and safety endpoints
- Health care resource utilization

The combination of the immunomodulatory agent pomalidomide with dexamethasone (pomal/dex) is an approved therapy for patients with advance-stage disease who have progressed after 2 prior lines of therapy.12 Although pom/dex therapy is a standard-of-care regimen for RRMM, an unmet need remains in this heavily pretreated patient population.

In the Phase 3 MM-003 trial in patients with RRMM receiving pom/dex results were:

- ORR of 33% (95% CI: 26.4, 40.6)
- Median PFS of 4.0 months (95% CI: 3.6, 4.7)

In the larger MM-010 (STRATUS) Phase 3b trial of pom/dex in RRMM results were:

- ORR of 33% (95% CI: 29.0, 36.2)
- Median PFS of 4.6 months (95% CI: 3.9, 4.9)

Pomalidomide/dexamethasone combination therapy

Trials in patients with RRMM receiving pom/dex:

- Median PFS of 12.0 months (95% CI: 9.8, 14.8)
- Median DoR of 14.3 months (95% CI: 10.6, NE)

In the Phase 3 STRATUS Phase 3b trial of pom/dex in RRMM results were:

- ORR of 60% (95% CI: 42.1, 76.1)
- Median PFS of 12.0 months (95% CI: 9.8, 14.8)
- Median DoR of 14.3 months (95% CI: 10.6, NE)

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- Prior BCMA-targeted therapy or pom treatment
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Key exclusion criteria:

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- Treatment with an anti-MM monoclonal antibody
- Prior BCMA-targeted therapy or pom treatment
- Prior allogeneic SCT

To evaluate the efficacy and safety of single-agent belantamab mafodotin compared with pom/dex, an established standard-of-care regimen in patients with RRMM treated with 2 prior lines of therapy.

Current status

Study start is planned for:

- Dec 2019

Presented at the American Society of Hematology Annual Meeting, Orlando, FL, USA, December 7–10, 2019

References