COMy

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Infection rate profile of etentamig monotherapy in patients with relapsed/refractory multiple myeloma

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OBJECTIVE

To evaluate the infection profile of a next generation B-cell maturation antigen (BCMA) bispecific antibody, etentamig, in a pooled analysis from two ongoing studies: a first-in-human phase 1 study and phase 1b study

CONCLUSIONS

The Grade 3/4 infection incidence rate of 23% was consistent with a best in class infection profile

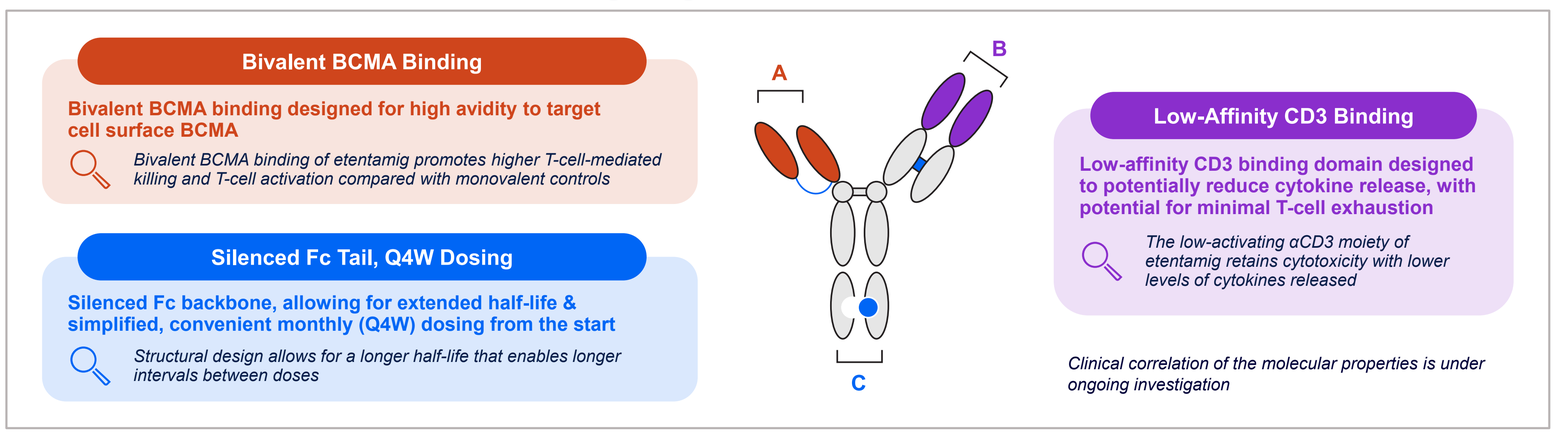
Infection-related discontinuation and Grade 5 infection rates were <5%

The favorable infection profile observed appears to result from etentamig's differentiated design, with the incorporation of a low-affinity CD3 binding domain

INTRODUCTION

- Multiple myeloma (MM) is a plasma cell malignancy characterized by clinical heterogeneity and multiple relapses[1]
- While current available immunotherapies have demonstrated potent efficacy, they come with increased risk of infections (especially airway infections) which can cause significant morbidity while increasing mortality risk[2–4]
- This important safety risk can cause implementation hesitancy, especially in a more resource constraint treatment setting, due to increased monitoring and prophylaxis needs, highlighting the need for treatment options that are not only efficacious but also have a more favorable infection risk profile
- Etentamig is being developed as a patient-centric, next generation differentiated BCMA x CD3 bispecific T-cell engager composed of a bivalent BCMA-binding domain with a high avidity, low-affinity CD3-binding domain potentially reducing cytokine release syndrome (CRS), and a silenced Fc tail for extended half-life enabling convenient monthly (Q4W) dosing from the start

Etentamig design and mechanism of action[5–8]



BCMA, B-cell maturation antigen; CRS, cytokine release syndrome; FcRn, neonatal Fc receptor; Q4W, every 4 weeks.

- Etentamig's low affinity CD3 binding in conjuction with the prolonged Q4W dosing interval minimizes T-cell exhaustion, compared with current available bispecific T-cell engagers, which may result in overall lower infection rates[5,9]
- Here, we present results from the ongoing first-in-human phase 1 and phase 1b (Arm A) studies of etentamig in patients with RRMM

METHODS

Data source

- This pooled analysis included data from a phase 1 multicenter, open-label, dose escalation/expansion (NCT03933735) trial and Arm A of a phase 1b, open label (NCT05650632) trial

Patients

Key inclusion criteria

- Adult patients with RRMM who received ≥3 prior lines of therapy, including exposure to a proteosome inhibitor, an immunomodulatory drug, and an anti-CD38 monoclonal antibody
- ECOG performance status ≤2

Key exclusion criteria

- Prior BCMA-targeted therapy

Etentamig treatment

- Patients in the phase 1 trial received 60 mg Q4W or 40 mg Q3W—with near equivalent dose intensities (60 mg Q4W dose intensity compared with 40 mg Q3W ≈ 1.125)— and no step-up-dosing
- Patients in Arm A of the phase 1b trial received a step-up dose on day 1 and full dose of 60 mg Q4W on day 4
- Study drug was administered until progressive disease, unacceptable toxicity, or other study discontinuation criteria were met

Assessments

- Pooled analysis assessed safety and tolerability
- Adverse events (AEs) were graded according to the NCI CTCAE Version 5.0

Supportive care

- Intravenous immunoglobulin (Ig) and anti-microbial prophylaxis were administered per institutional guidelines

RESULTS

Patient population and demographics

- Of 146 patients with RRMM who received etentamig, 87 (60%) were male, median age (range) was 68 (40–87) years, median prior lines of therapy were 4 (3–23)
- As of July 12, 2024 (data cutoff), the median duration of follow-up was 13 (1–48) months

Pooled demographic and baseline disease characteristics

Characteristics	Total (N=146)
Median age, years (range)	68 (40–87)
Sex, n (%)	
Male	87 (60)
Female	59 (40)
Race, n (%)	
White	112 (77)
Black or African American	24 (17)
Asian	4 (3)
ECOG performance status, n (%)	
0	61 (42)
1	127 (87)
2	17 (12)
R-ISS stage at study entry, n (%)	
I	34 (23)
II	78 (53)
III	29 (20)
High-risk cytogenetics[a], n (%)	38 (26)
Extramedullary plasmacytoma, n (%)	
Presence	22 (22)
Absence	113 (78)
Median prior lines of therapy (range)	4 (3–23)
Prior cancer therapy, n (%)	
Triple-class refractory	112 (77)
Penta-drug refractory	48 (33)
Baseline hypogammaglobulinemia, n (%)	81 (56)

[a]Defined as one or more of t(4;14), t(14;16), or del(17p) detected via FISH. ECOG PS, Eastern Cooperative Oncology Group performance status; R-ISS, Revised International Staging System.

Etentamig Grade 3/4 infection profile

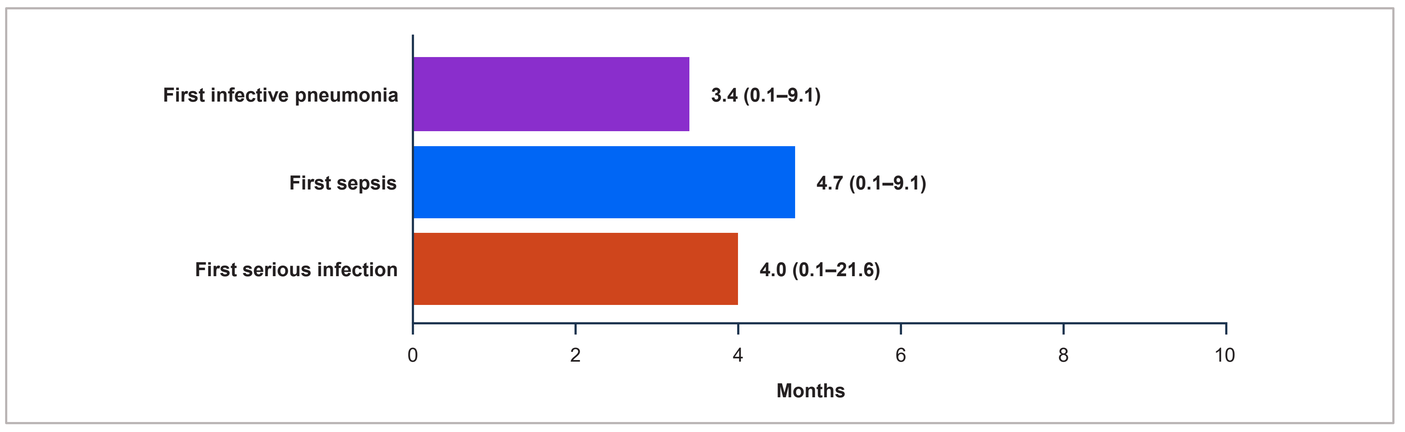
Adverse event, n (%)	N=146
Any Grade 3/4 infection	33 (23)
Infective pneumonia	23 (16)
Sepsis	9 (6)
Respiratory infection[a]	
Sinusitis	3 (2)
Upper respiratory tract infection	2 (1)
COVID-19	2 (1)
Bronchitis	1 (<1)
Urinary tract infection	2 (1)
Gastrointestinal infection	
Diverticulitis	1 (<1)
Clostridium difficile colitis	1 (<1)
Campylobacter gastroenteritis	1 (<1)
Osteomyelitis	1 (<1)
Varicella zoster virus	1 (<1)
Infections leading to etentamig discontinuation	6 (4)

[a]Excludes infective pneumonia.

Safety

- Serious infections occurred in 35 (24%) patients, pneumonia (12% [n=17]) and sepsis (6% [n=8]) were most common
- Grade 3/4 infections occurred in 23% (n=33) of patients; the most common were pneumonia (16% [n=23]) and sepsis (6% [n=9])
- Neutropenia (38% [n=56]) was the most common Grade 3/4 hematologic TEAE
- Overall, hypogammaglobulinemia (≥1 postbaseline IgG level <400 mg/dL) was reported in 87% (n=127) of patients
- One (0.7%) TEAE of opportunistic infection (Grade 2 cytomegalovirus reactivation) was reported
- Infection-related drug interruptions and discontinuations occurred in 48 (41%) and 6 (4%) patients, respectively
- Deaths from infections without intervening post-myeloma treatment were reported in 3% (n=4) of patients
  - Deaths were due to sepsis (n=3) and COVID-19 pneumonia (n=1; potentially related to study drug)

Time to infection onset, median (range)



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