Efficacy and safety of the DLL3 T-cell engager gocatamig in participants with neuroendocrine prostate cancer and other neuroendocrine neoplasms

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KEY STUDY OBJECTIVES

Primary

- Assess the safety and tolerability of gocatamig monotherapy
- Estimate the maximum tolerated dose of gocatamig monotherapy and determine the recommended dose(s) for expansion
- Characterize the pharmacokinetics of gocatamig monotherapy

Secondary

- Evaluate the preliminary efficacy of gocatamig monotherapy
- Evaluate the immunogenicity of gocatamig monotherapy

CONCLUSIONS

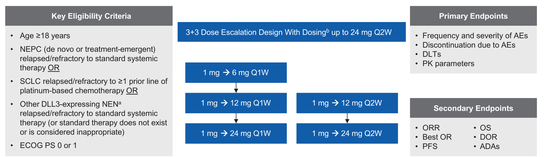
- Gocatamig monotherapy shows encouraging clinical activity in participants with NEC, including heavily pretreated GU NEC, with 24 mg Q2W emerging as the preferred monotherapy dosage
  - Confirmed ORR was 17.4% for participants with NEPC (30.0% for those treated at 24 mg Q2W) and 33.3% for participants with SCCB
- Clinical activity was observed in GU NEC across all DLL3 expression levels
- TRAEs were manageable, with most CRS cases being grade 1 or 2
  - Discontinuation of gocatamig due to TRAEs was infrequent
- Investigations of gocatamig as monotherapy and as part of combination regimens with other cancer therapies, including ifinatamab deruxtecan, atezolizumab, and durvalumab, are ongoing

BACKGROUND

- Genitourinary neuroendocrine carcinomas (GU NEC), including small cell carcinoma of the bladder (SCCB) and neuroendocrine prostate cancer (NEPC), are highly aggressive neuroendocrine neoplasms (NEN) with poor prognosis and limited treatment options[1,2]
- Delta-like ligand 3 (DLL3) expression is frequently upregulated in NEPC and other high-grade NEN but not in normal tissues[3]
- Gocatamig (MK-6070; HPN328) is a DLL3-directed T-cell engager[4]
- Gocatamig monotherapy has shown promising clinical activity and manageable safety in the treatment of DLL3-expressing tumors, including small cell lung cancer (SCLC)[5,6]
- Here we report updated results of safety, tolerability, and preliminary efficacy for participants with NEPC and other NEN treated with gocatamig monotherapy in the ongoing phase 1/2 study 6070-001

METHODS

Figure 1. Phase 1/2 6070-001 (NCT04471727) study design (gocatamig monotherapy cohorts)



[a]Other NEN were high-grade neuroendocrine tumors or NEC. [b]The target dose of 12 mg was administered Q1W or Q2W following a single priming dose of 1 mg. The target dose of 24 mg was administered Q1W or Q2W following a single priming dose of 1 mg and a step-up dose of 12 mg.
ADA, antidrug antibody; AE, adverse event; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; OR, overall response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; Q1W, once every week; Q2W, once every 2 weeks.

- Adverse events (AEs) were graded based on the NCI CTCAE v5.0, except for cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS), which were graded based on the American Society for Transplantation and Cellular Therapy 2019 criteria
- Preliminary analysis of efficacy was based on investigator's assessment per RECIST v1.1 (ORR, PFS, and DOR) and Prostate Cancer Working Group 3 criteria for NEPC (ORR and DOR)
- DLL3 testing was performed centrally using the Ventana DLL3 (SP347) assay at Mayo Clinic Laboratories or DCL Pathology, and staining was scored internally by a pathologist at Merck & Co., Inc.
  - DLL3 (high): ≥50% tumor cell staining at moderate and/or strong intensity
  - DLL3 (low): <50% tumor cell staining at moderate and/or strong intensity
  - DLL3 (zero): DLL3 expression absent or weak staining

RESULTS

- Results presented are for 60 participants with NEPC or other NEN in dose cohorts with 1-mg priming dose and target doses of 6 mg Q1W, 12 mg Q1W and Q2W, and 24 mg Q1W and Q2W
  - Results for participants with SCLC are not shown
- Data cutoff was on August 29, 2025
- Median time from the date of first dose to the date of data cutoff was 19.1 months (range 3.8-33.3)

Table 1. Baseline demographics and clinical characteristics

Participants treated (Dose escalation with 1-mg priming dose; N=60)			
Diagnosis, n (%)			
NEPC	23 (38)		
Other NEN	37 (62)		
SCCB	12 (20)		
Baseline demographics and clinical characteristics	**NEPC (n=23)**	**Other NEN[a] (n=37)**	**Total (N=60)**
Median (range) age, years	68 (47-82)	61 (37-79)	63 (37-82)
Male, n (%)	23 (100)	22 (59)	45 (75)
ECOG PS, n (%)			
0	13 (57)	17 (46)	30 (50)
1	10 (43)	20 (54)	30 (50)
Median (range) prior lines of therapy	3 (1-7)	2 (1-6)	3 (1-7)
≥3 prior lines of therapy, n (%)	17 (74)	15 (41)	32 (53)
Prior anti-PD-(L)1 therapy, n (%)	15 (65)	25 (68)	40 (67)
Prior platinum therapy, n (%)	23 (100)	36 (97)	59 (98)
Sites of metastases, n (%)			
Brain	6 (26)	13 (35)	19 (32)
Liver	16 (70)	18 (49)	34 (57)

[a]Includes 12 participants with SCCB.

Table 2. Summary of treatment-related adverse events (TRAEs)

Participants, n (%)	NEPC (n=23)	Other NEN[a] (n=37)	Total (N=60)
Any TRAE	23 (100)	36 (97)	59 (98)
Grade 3-5	11 (48)	14 (38)	25 (42)
Serious	13 (57)	10 (27)	23 (38)
Fatal	0	0	0
Discontinued treatment	0	1 (3)	1 (2)

[a]Includes 12 participants with SCCB.

Table 3. Summary of the most common TRAEs (any-grade incidence ≥20% in the total population[a])

Participants, n (%)	NEPC (n=23)	Other NEN[b] (n=37)	Total (N=60)
CRS, any grade	22 (96)	23 (62)	45 (75)
Grade 3-5	*1 (4)*	*1 (3)*	*2 (3)*
Fatigue, any grade	13 (57)	21 (57)	34 (57)
Grade 3-5	*1 (4)*	*0*	*1 (2)*
Dysgeusia, any grade	14 (61)	19 (51)	33 (55)
Vomiting, any grade	10 (43)	16 (43)	26 (43)
Nausea, any grade	8 (35)	16 (43)	24 (40)
Diarrhea, any grade	7 (30)	12 (32)	19 (32)
Grade 3-5	*0*	*4 (11)*	*4 (7)*
Decreased appetite, any grade	6 (26)	13 (35)	19 (32)
Grade 3-5	*0*	*1 (3)*	*1 (2)*
Constipation, any grade	7 (30)	7 (19)	14 (23)
Hyponatremia, any grade	8 (35)	5 (14)	13 (22)
Grade 3-5	*2 (9)*	*1 (2.7)*	*3 (5)*
AST increased, any grade	5 (22)	7 (19)	12 (20)
Grade 3-5	*1 (4)*	*0*	*1 (2)*
Pruritus, any grade	5 (22)	7 (19)	12 (20)
Weight decreased, any grade	4 (17)	8 (22)	12 (20)
Grade 3-5	*0*	*1 (3)*	*1 (2)*
Headache, any grade	4 (17)	8 (22)	12 (20)
Grade 3-5	*0*	*1 (3)*	*1 (2)*

[a]TRAEs with no grade 3-5 events are not shown.
[b]Includes 12 participants with SCCB. AST, aspartate aminotransferase.

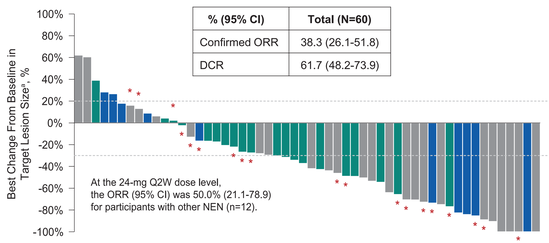
Table 4. Summary of CRS/ICANS events by highest grade

Participants, n (%)	NEPC (n=23)	Other NEN[a] (n=37)	Total (N=60)
CRS, any grade	22 (96)	23 (62)	45 (75)
Grade 1	16 (70)	16 (43)	32 (53)
Grade 2	5 (22)	6 (16)	11 (18)
Grade 3-4[b]	1 (4)	1 (3)	2 (3)
ICANS, any grade	3 (13)	2 (5)	5 (8)
Grade 1	2 (9)	0	2 (3)
Grade 2	0	2 (5)	2 (3)
Grade 3-4[b]	1 (4)	0	1 (2)

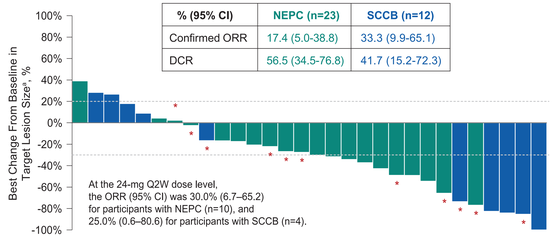
[a]Includes 12 participants with SCCB. [b]There were no Grade 5 events of CRS or ICANS.

Figure 2. Best percentage change from baseline in target lesion size for (A) the total population (N=60) and (B) participants with GU NEC (n=35)

A. Participants with NEPC (teal), SCCB (blue), or all other tumor types (gray)



B. Participants with NEPC (teal) or SCCB (blue)



[a]Among participants who received any amount of study treatment and had at least one postbaseline scan. Asterisks (*) indicate treatment at the 24-mg Q2W dose level.
DCR, disease control rate.

Figure 3. Duration of treatment and response among participants with NEPC (teal) and SCCB (blue)

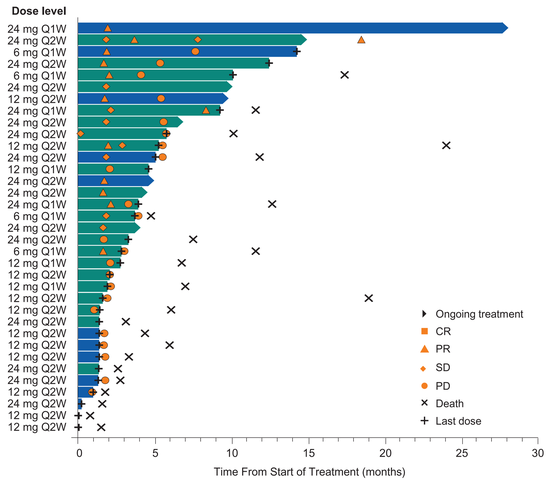


Figure 4. Change in target lesion size over time among participants with NEPC (teal) and SCCB (blue)

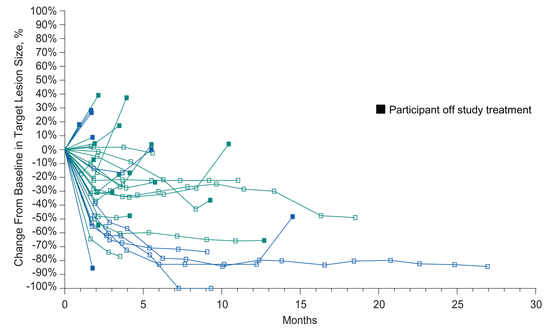


Table 5. Efficacy by DLL3 expression level in GU NEC among participants with NEPC and SCCB with staining available

	NEPC (n=19)			SCCB (n=9)		
% (95% CI)	DLL3 (high) (n=11)	DLL3 (low) (n=8)	DLL3 (zero)[a] (n=1)	DLL3 (high) (n=5)	DLL3 (low) (n=4)	DLL3 (zero)[a] (n=0)
Confirmed ORR	18 (2.3-51.8)	25 (3.2-65.1)	100 (2.5-100)	40 (5.3-85.3)	25 (0.6-80.6)	NA
DCR	55 (23.4-83.3)	63 (24.5-91.5)	100 (2.5-100)	40 (5.3-85.3)	25 (0.6-80.6)	NA

[a]DLL3 (zero) is a subset of DLL3 (low).
NA, not applicable.

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