Preliminary data from QUILT 3.055: a phase 2 multi-cohort study of N803 (IL-15 superagonist) in combination with Checkpoint Inhibitors (CPI)

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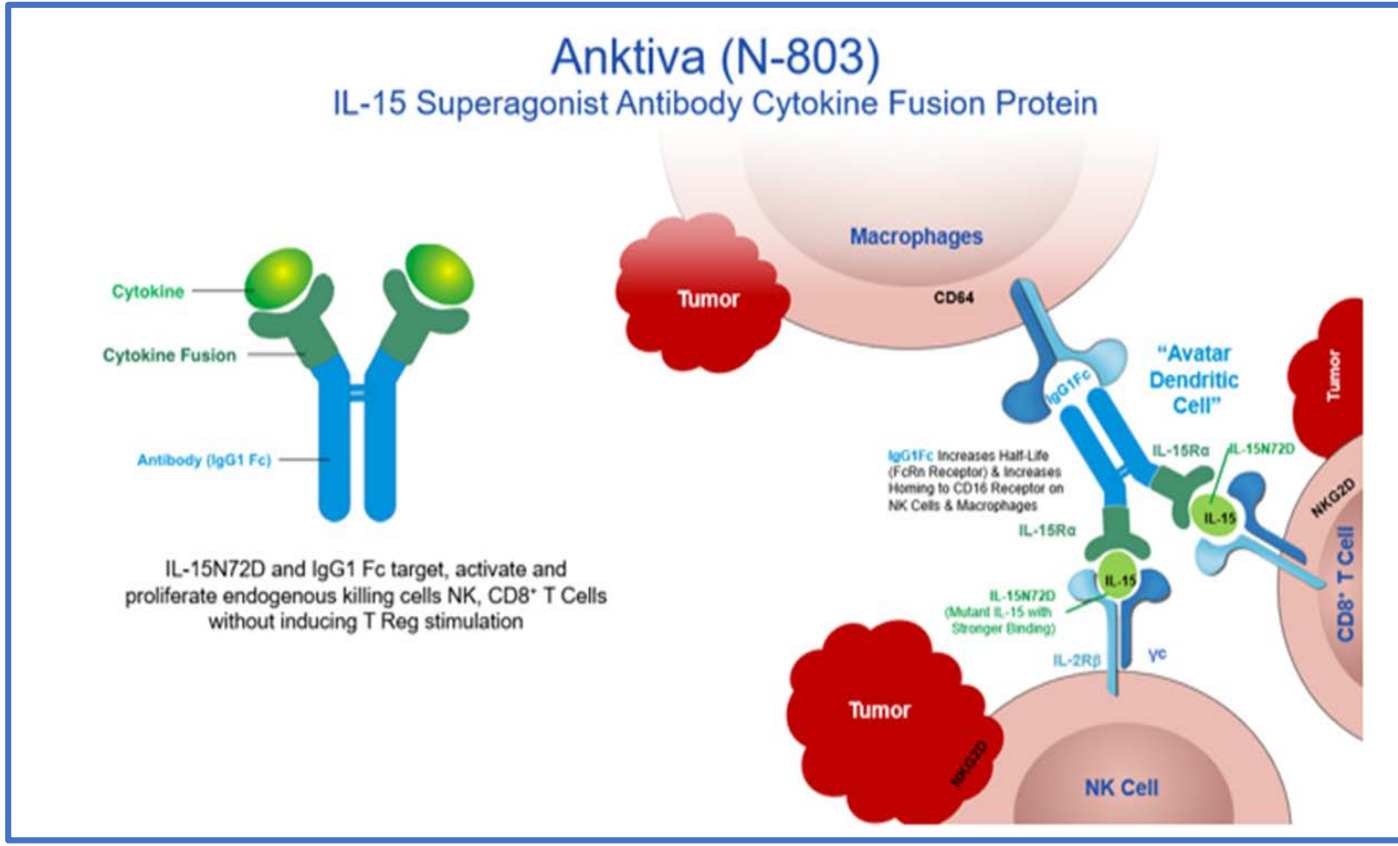
June 2021

BACKGROUND

- N-803 (IL-15 fusion protein) – activates NK and CD8+ T cells without activation of Treg cells
- Fc backbone extends half-life beyond native IL-15
- N72D mutation enhances IL-15 binding
- Trans presentation of IL-15 to IL-2 receptor beta/gamma

STUDY DESIGN

- SOC CPI (Nivo, Pembro, Atezo, Avelumab) at FDA dose/schedule
- N803 15 ug/kg SQ q3 or q4 weeks (to mirror CPI)
- Study entry required active RECIST progression on CPI as last line of therapy



Checkpoint Inhibitor containing regimen 2nd or 3rd line

CR/PR/6 month stable disease

PROGRESSION

N803 (15ug/kg SC) + same checkpoint inhibitor

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Cohort 1 Patients with initial response on single-agent checkpoint inhibitor therapy and subsequently progressed on or after that therapy:

1a Non-small cell lung cancer (NSCLC)
1b Small cell lung cancer (SCLC)
1c Urothelial carcinoma
1d Head and neck squamous cell carcinoma (HNSCC)
1e Merkel cell carcinoma (MCC)
1f Melanoma (single PD-1/PD-L1 checkpoint inhibitor therapy or in combination with ipilimumab)
1g Renal cell carcinoma (RCC)
1h Gastric cancer
1i Cervical cancer
1j Hepatocellular carcinoma (HCC)
1k Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumor cancer or colorectal cancer (CRC)

Cohort 2 Patients having high PD-L1 expression (tumor proportion score [TPS] ≥50%) and disease progression on a PD-1 checkpoint inhibitor after experiencing an initial response when received checkpoint inhibitor as a single-agent for first-line treatment of NSCLC.

Cohort 3 Patients with initial response but subsequently relapsed on maintenance PD-1 checkpoint inhibitor therapy when initially received checkpoint inhibitor therapy in combination with chemotherapy as first-line treatment of NSCLC.

Cohort 4 (exploratory) Patients currently receiving PD-1/PD-L1 checkpoint inhibitor therapy and have progressed after experiencing stable
disease for at least 6 months during previous treatment with PD-1/PD-L1 checkpoint inhibitor therapy. Indication includes: NSCLC, HNSCC, RCC, Urothelial carcinoma

Adverse Event Profile

Treatment-Related AE's

Cohort	Any Grade	Grade 1-2	Grade 3	Grade 4	Grade 5
Cohort 1a (N=19)	15	12	1	1	1
Cohort 1b (N=10)	8	7	1	0	0
Cohort 1c (N=1)	1	0	1	0	0
Cohort 1d (N=8)	6	4	2	0	0
Cohort 1f (N=15)	13	11	2	0	0
Cohort 1g (N=8)	7	7	0	0	0
Cohort 1h (N=3)	2	1	1	0	0
Cohort 1i (N=2)	2	1	1	0	0
Cohort 2 (N=10)	9	7	2	0	0
Cohort 3 (N=19)	19	17	2	0	0
Cohort 4 (N=44)	35	31	4	0	0
All Subjectss A (N=140)	117 (84%)	98 (70%)	17 (12%)	1 (<1%)	1 (<1%)

Treatment-Related SAE's

8%

Common low grade AEs were: injection site reaction (71%), chills (34%), fatigue (27%), pyrexia (24%), nausea (14%), flu-like Illness (13%), decreased appetite (10%), all others were <10% incidence. Grade 3+ AEs: injection site reaction (1%), maculo-popular rash (1%), ALT/AST/Alk phos increase (1%), fatigue (<1%), anemia (1%), sepsis (<1%), pneumonitis (<1%), DVT(<1%), hypovolemic shock (<1%), colitis (<1%), diarrhea (<1%), delirium (<1%). *Grade 5: Respiratory failure (<1%) after 1 dose of N803 and attributed to CPI and N803

Clinical Efficacy Profile

	NSCLC	Small Cell	Urothelial	H&N	Melanoma	Renal	Gastric	Cervix	Cohort 2	Cohort 3	Cohort 4	*ALL*
N	19	10	1	8	15	8	3	2	10	19	44	*140*
PR	3 (16%)	1 (10%)	0	2 (25%)	1 (7%)	0	0	2 (100%)	0	1 (5%)	3 (7%)	*13 (9%)*
SD	9 (47%)	2 (20%)	1 (10%)	4 (50%)	5 (33%)	6 (75%)	2 (67%)	0	6 (60%)	11 (58%)	23 (52%)	*69 (49%)*
PD	5 (26%)	5 (50%)	0	0	6 (40%)	1 (13%)	0	0	2 (20%)	7 (37%)	13 (30%)	*39 (28%)*
NA	2 (11%)	1 (10%)	0	2 (25%)	3 (20%)	1 (13%)	1 (33%)	0	2 (20%)	0	5 11%)	*19 (14%)*

SD = minimum 6 weeks of SD , 36% of all subjects experienced SD >2 months & 16% SD >6 months, NA = no response assessment to date. Response assessment includes unconfirmed PRs. No Complete responses were seen.

CONCLUSIONS

- N803 exhibits a favorable toxicity profile in combination with multiple different checkpoint inhibitors in 2nd line or greater settings across a variety of tumor types
- AE rates (12% grade 3 or above) of the chemo-free combination were better than historical standard of care alternative of combination chemotherapy
- Clinical benefit in the majority of subjects, with cessation of progression, prolonged stable disease, and occasional RECIST partial responses were seen across different tumor types