Abstract #396754

Quality of Life in the QUILT 3032 Study: BCG-Unresponsive Non-Muscle Invasive Bladder Cancer (NMIBC) Patients Receiving IL-15 Superagonist N-803 Plus BCG

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BACKGROUND

Patients (pts) with bacillus Calmette-Guerin (BCG)-unresponsive NMIBC have limited treatment options and are at an increased risk for cystectomy. N-803 (nogapendekin alfa inbakicept: Anktiva®), is an interleukin-15 superagonist (IL-15) [1], which synergizes with BCG to elicit durable complete responses (CRs) in this patient population [2].

In the open-label, 3-cohort, multicenter phase 2/3 study QUILT 3032 (NCT03022825), pts with BCG-unresponsive bladder carcinoma in situ (CIS) with or without Ta/T1 disease (Cohort A) treated with N-803 and BCG had a CR rate of 71% (median duration 26.6 months), 90% cystectomy avoidance in those with a CR and 100% bladder cancer-specific survival at 24 months*.

To facilitate more meaningful comparison of BCG+N-803 therapy to other available therapies and potentially identify variables that may affect patient-reported outcomes, participants in QUILT 3032 were asked to complete quality-of-life (QoL) questionnaires. Here, we present QoL findings for hospitalizations, feeling ill, global health (GH), physical function (PF), and summary scores from the NMIBC-specific questionnaire.

*January 15, 2022 cutoff

METHODS

QoL was assessed by the EORTC (www.qol.eortc.org) QoL Questionnaire Core 30 (QLQ-C30) and QoL NIMBC-Specific 24 Questionnaire (QLQ-NMIBC24) in cohort A pts (n = 86)**, treated with intravesical BCG+N-803 weekly for 6 consecutive weeks; patients who did not achieve a CR by the week 12 assessment were offered re-induction. Here, scores for GH and PF were compared for all patients at 0, 6, 12, 18 and 24 months***, for those with CR vs. without a CR - and for 11 summary scores on the QLQ-NMIBC24 - at 0, 6 and 12 months. To assess the influence of baseline clinical variables of age (<65 or ≥ 65 yrs), gender (F, M), race (white, non-white), baseline disease type (CIS, CIS/Ta, CIS/T1), baseline ECOG (0, 1-2), number of prior BCG doses (<12, ≥12), prior cancer therapy (BCG, BCG + other therapy), number of prior transurethral resection of the bladder tumor (TURBT; ≤3, >3), and non-baseline variable CR or no CR on GH, PF, as well as summary scores from the QLQ-NMIBC24, a multivariate regression model was used wherein change from baseline score was the dependent variable, baseline QoL score was included as a covariate, and baseline clinical variables included as independent variables. The multivariate analyses were conducted on month 6 and 12 scores.

**Cohort A: median age 73 years; 87% male; 82% had an ECOG score = 0.

***May 16, 2022 cutoff

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FINDINGS

Table 1. Feeling ill or unwell by visit (n, %)

	Baseline	Month 6	Month 12	Month 18	Month 24
n#	86	66	50	46	35
Not at all	82, 95.4%	58, 87.9%	46, 92.0%	43, 93.5%	32, 91.4%
A little	4, 4.7%	8, 12.1%	3, 6.0%	2, 4.4%	2, 5.7%
Quite a bit	0, 0%	0, 0%	1, 2.0%	1, 2.2%	0, 0%
Very much	0, 0%	0, 0%	0, 0%	0, 0%	1, 2.9%

- On-study hospitalizations for any reason were low at 0%-6%.
- Participant QoL form completion rate was high, being 90% or greater at most time points.
- Patient reports of 'feeling ill' or 'unwell' increased at month 6, but returned to near baseline levels at months 12, 18 and 24 (**Table 1**).
- There was a modest decrease in mean PF and GH from baseline at all assessed on-study time points that became less by month 24 (**Fig. 1A**).
- When responders (those with a CR) were compared with non-responders, they showed less of a decrease in PF (**Fig. 1B**) and GH (**Fig. 1C**) scores with time, although both parameters were higher at baseline for responders.
- In multivariate analysis, at month 12, >3 prior TURBT was significantly (p = .0729; cutoff ≤ .1) associated with lower GH scores as compared with ≤3 prior TURBT (**Table 2**).
- At month 6, achievement of a CR was significantly (p = .0659) associated with higher PF scores as compared with no CR (**Table 2**).
- No other baseline variable had significant level of association (min. p-value = 0.1076).
- Several variables were significantly associated with QLQ-NMIBC24 summary scores (**Table 3**) with achievement of a CR being associated with higher scores for questions related to sexual activity.

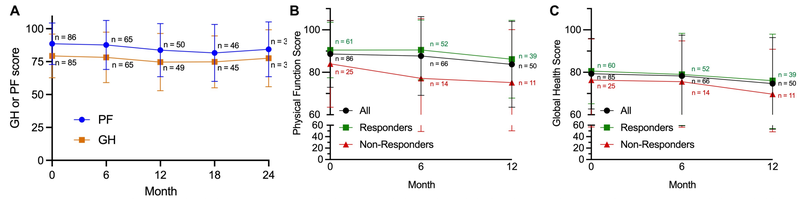

Fig. 1 *Physical function (PF) & global health (GH) scores.* (A) PF (blue) & GH (orange) scores for all patients. (B) PF & (C) GH scores (mean & SD) for all (black), responders (green), & non-responders (red) at baseline, month 12 and 24.

Table 2. Multivariate Analysis

	Parameter							
	Global Health				Physical Function			
Variable	p-value (mo. 6)	Est.	p-value (mo. 12)	Est.	p-value (mo. 6)	Est.	p-value (mo. 12)	Est.
Age (***<65***, ≥65 yrs)	0.6428	-2.79	0.9199	1.23	0.9853	-0.10	0.9723	0.32
Sex (***F***, M)	0.6077	-4.83	0.9638	-0.68	0.9110	0.9100	0.7454	-3.70
Race (***white***, non-white)	0.7674	2.69	0.8969	-2.39	0.3249	-7.07	0.9101	-1.30
Baseline disease type** CIS/T1	0.9474	0.56	0.696	7.05	0.7149	2.73	0.2477	14.53
Baseline disease type** CIS/Ta	0.1076	-10.13	0.3498	-11.46	0.8636	-0.95	0.7906	-2.58
Baseline ECOG (***0***, 1-2)	0.7968	1.90	0.5252	-8.82	0.8443	-1.34	0.2787	-12.16
#Prior BCG doses (***<12***, ≥12)	0.4691	-4.45	0.1803	16.35	0.6797	2.23	0.2417	10.65
Prior cancer therapy***	0.3063	-4.81	0.5207	6.58	0.2233	-5.00	0.9606	0.36
#Prior TURBT (***≤3***, >3)	0.5769	-2.71	**0.0729**	-17.69	0.4839	3.2	0.6346	-3.78
CR or ***no CR*****	0.3324	5.36	0.4396	8.3	**0.0659**	9.18	0.489	5.98

The reference groups are indicated in **bold italics. Mo. - month; Est. – estimate; **reference group is **CIS**; ***reference group is **BCG only**, compared with BCG+other therapy; ****CR - complete response (not baseline)*

Table 3. Multivariate Analysis of QLQ-NMIBC24 Summary Scores

Question	Variable	p value, mo 6	Est.	p value, mo 12	Est.
Urinary symptoms	Age (***<65***, ≥65 yrs)			0.0238	-23.03
	Sex (***F***, M)			0.0287	26.76
Malaise	Race*	0.0470	-6.21		
Bloating & flatulence	Baseline disease type **CIS/T1			0.0090	-25.91
Intravesical Tx issues	Age (***<65***, ≥65 yrs)			0.0412	-26.64
Sexual function	CR or ***no CR*****	0.0110	16.65	0.0364	22.87
	Sex (***F***, M)	0.0316	-109.48		
	Race*	0.0224	89.87		
Sexual intimacy	Baseline disease type CIS/Ta	0.0365	-50.65		
	#Prior TURBT (***≤3***, >3)	0.0170	-58.82		
	CR or ***no CR*****	0.0137	75.82		
Sexual problems, M	CR or ***no CR*****	0.0153	-30.60		

*Reference groups in **bold italics**. Mo. - month; Est - estimate, ***white**, non-white; ****CIS**, CIS/Ta, CIS/T1; ***CR- complete response (not baseline)*

- Overall, summary scores for the QLQ-NMIBC24 questionnaire concerning urinary symptoms, malaise, future worries, bloating & flatulence, intravesical treatment issues, sexual function, sexual intimacy, risk of contaminating partner, sexual enjoyment, and sexual problems (male, female) remained stable from baseline to months 6 & 12

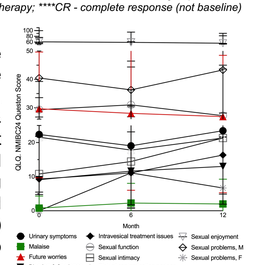

Fig. 2 *QLQ-NMIBC24 summary scores (mean & SD).*

CONCLUSIONS

- Patient reports of 'feeling ill' or 'unwell' remained near baseline levels at months 12, 18, and 24 after N-803 plus BCG.
- Physical function and global health remained stable from baseline through 24 months.
- Overall, summary scores for the NMIBC-specific questions remained stable through 12 months.
- A positive difference in physical function in responders versus non-responders was noted.
- Taken together, these findings indicate a favorable risk/benefit ratio and quality of life following N-803 plus BCG, comparable to BCG alone [3-5].

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References
1. Han, et al. 2011 Cytokine 56:804-810. DOI:10.1016/j.cyto.2011.09.028.
2. Chamie, Chang, et al. 2022 NEJM Evidence; DOI:10.1056/EVIDoa2200167.
3. Catto, et al. 2020 Journal of Clinical Oncology, 39 (3); DOI:10.1200/JCO.20.01665
4. Nayak, et al. 2021 Transl Androl Urol 2021;10(6); DOI:10.21037/tau-20-1333
5. Yuen, et al. 2022 Intl J. Environ. Res. Public Health 19; DOI:10.3390/ijerph191710825