

Drivers of Treatment Preferences in High-risk Non-muscle Invasive Bladder Cancer (HR-NMIBC) Patients: Qualitative Interviews to Inform a Patient-Preference Study

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Objective

Qualitative interviews were conducted with patients with high-risk non-muscle invasive bladder cancer (HR-NMIBC) to explore perspectives regarding treatments to inform the development of a quantitative patient preference study (discrete choice experiment [DCE]).



Key findings and conclusions

- Efficacy (event-free survival) was a key driver of treatment choice among patients with HR-NMIBC.
- Patients also considered adverse events (AEs) (i.e., bladder problems, serious immune-related AEs, the likelihood of developing chronic conditions, such as diabetes and adrenal insufficiency), and route of administration to be important. The possibility of experiencing thyroid problems, flu-like symptoms, and the overall duration of a treatment course were of lesser importance.
- Findings from the qualitative interviews informed attribute and level selection (in conjunction with input sought via an expert clinician and a patient advocate) and provided supportive evidence that planned attributes and constituent levels are considered meaningful to a HR-NMIBC patient population.



Considerations

- Capturing and incorporating the patient perspective (via qualitative research) as part of the design and development of quantitative patient preference studies is critical for ensuring the validity and relevance of resulting data for the specific decision-making context.
- Qualitative research findings highlight the value of conducting future quantitative preference elicitation (e.g., via a DCE) to quantify relative attribute importance, and the trade-offs patients are willing to make among attributes of treatment for HR-NMIBC.
- Final attributes and levels may be subject to modifications based on survey pilot testing, major changes in the treatment landscape, among other considerations.

Background

- Non-muscle invasive bladder cancer (NMIBC) represents 75% of bladder cancer diagnoses.¹
- Intravesical instillation of Bacillus Calmette-Guerin (BCG) is the standard of care (SOC) in high-risk NMIBC (HR-NMIBC); though for many patients the disease may recur or progress to more life-threatening muscle-invasive disease.^{2,3}
- Additionally, estimates indicate many patients do not adhere to or complete recommended BCG schedules due to side effects, administration burden, and tumor progression/recurrence.^{4,5}
- Several investigational therapies (e.g., immune-checkpoint inhibitors [ICI]) such as programmed death-ligand 1 (PD-L1) are being studied in randomized control trials (RCTs) in HR-NMIBC patients.
- Differences may exist with regards to administration, safety, and efficacy between monotherapy options and combination regimens comprising PD-(L)1s and SOC.
- Currently, evidence (both qualitative and quantitative) on the importance of different treatment attributes from the perspective of HR-NMIBC patients is limited.
- This study aimed to explore HR-NMIBC patient perspectives on BCG and PD-(L)1 treatment attributes, to inform the development and refinement of an attributes and levels (A&L) grid to be used in a discrete choice experiment (DCE).

Materials and Methods

DEVELOPMENT OF AN ATTRIBUTES AND LEVELS (A&L) GRID

- A draft attributes and levels (A&L) grid comprising 11 attributes (**Figure 1**) was developed following a targeted literature review (TLR) and consultation with an expert urologist and a patient advocate.
- The draft grid included attributes reflecting safety, administration and survival outcomes of approved and investigational HR-NMIBC therapy options.
- Development and testing of the A&L grid aligned with best methodological practice⁶⁻⁸ and regulatory guidance.⁹⁻¹¹

QUALITATIVE INTERVIEWS:

- 90-minute telephone interviews were conducted by three trained interviewers with US patients with HR-NMIBC recruited via patient advocacy groups (PAGs).
- The interviews utilized a semi-structured discussion guide. A variety of qualitative approaches were employed:¹²

Concept elicitation (CE)	Open-ended questioning to explore patient experience and perspectives regarding treatment and drivers for treatment choice
Cognitive debriefing (CD)	Structured probed questioning to assess patient comprehension of the A&L grid (provided to patients for review during the interview) and to evaluate if attributes and associated levels represented concepts considered important in patient treatment decision-making (content validity)
Treatment choice tasks	Fixed profile choice tasks to assess usability/feasibility of the task layout/format, and to obtain preliminary qualitative insights into trade-offs between attribute levels
Ranking exercise	Patients ranked the most and least important attributes in the A&L grid
Rated importance exercise	Patients rated the importance of each attribute on a 0-10 numeric rating scale (NRS) – 0 = not at all important, 10 = very important.

QUALITATIVE ANALYSIS

- Interviews were audio-recorded and transcribed verbatim. Transcripts were coded in ATLAS.ti²² and analyzed using thematic analysis methods.¹²
- For CE data, an iterative inductive-deductive approach enabled prior theory and knowledge to identify themes¹³ while capturing new themes identified in the interviews.¹⁴
- For CD data, a pre-defined coding structure was used to apply dichotomous codes (e.g., YES/NO) to indicate if an attribute or level was understood/interpreted correctly, important, and meaningful.

Results

STUDY SAMPLE

- A total of 12 patients with clinician-confirmed (n=6) or self-reported (n=6) HR-NMIBC were recruited. All patients had received BCG therapy (**Table 1**).

Table 1. Patient demographic and clinical characteristics (N=12)		
Description		Total sample, N=12
Age	Median	64
years	Min/Max	54–78
Gender		
n (%)	Male	7 (58.3%)
	Female	5 (41.7%)
Ethnic origin		
n (%)	Caucasian	11 (91.7%)
	Hispanic or Latino	1 (8.3%)
Highest level of education		
n (%)	High school or equivalent	2 (16.7%)
	Associate's Degree	2 (16.7%)
	Bachelor's Degree	4 (33.3%)
	Master's Degree	2 (16.7%)
	Doctorate	2 (16.7%)
Employment status		
n (%)	Working full time	5 (41.7%)
	Working part time	2 (16.7%)
	Retired	5 (41.7%)
Current control of NMIBC		
n (%)	Fair	4 (33.3%)
	Good	6 (50.0%)
	Excellent	2 (16.7%)
Time since NMIBC diagnosis		
n (%)	≤1 year	5 (41.7%)
	>1-2 years	3 (25.0%)
	>2-3 years	4 (33.3%)
Number of BCG sessions		
n (%)	Induction (≤6 sessions)	5 (41.7%)
	Maintenance (>7 sessions)	7 (58.3%)
Received chemotherapy for NMIBC		
n (%)	Yes	6 (50.0%)
	No	6 (50.0%)

CONCEPT ELICITATION: TREATMENT DRIVERS

- When asked to describe an ideal treatment for HR-NMIBC, patients spontaneously discussed the importance of *route of administration* (n=11/12). Specifically, most patients reported a preference for a treatment in either 'pill/tablet' form (n=6/11) or as an 'injection' (n=3/11).
- Treatment efficacy (framed as event-free survival) (n=10/12), *a favorable dosing schedule* (n=8/12), and *mitigation of side-effects* (n=7/12) were also spontaneously discussed as important attributes.

"Well I think the ideal treatment would be some sort of an, an oral medication, a pill that I could take, you know, once a day" (**Patient 1**)

"The result would be-the outcome would be basically that, uh, the cancer is in remission. That, uh, they, they do-there's nothing there to see and the cancer hasn't spread anywhere else." (**Patient 10**)

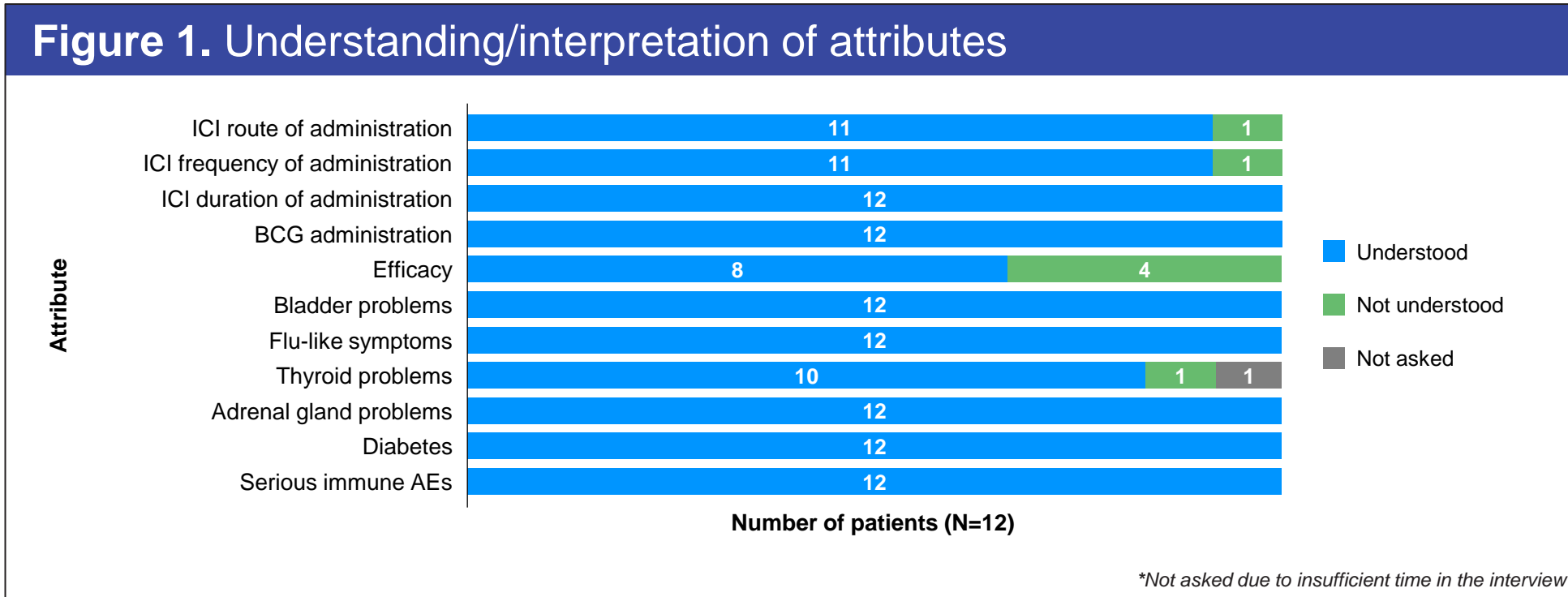
COGNITIVE DEBRIEFING (CD) OF THE DRAFT A&L GRID

Understanding and interpretation

- Most attributes in the draft A&L grid were generally well understood and interpreted as intended (**Figure 1**).
- One third of patients (n=4/12) did not interpret the draft efficacy attribute in the way that was intended.
 - The specific areas of misinterpretation included interpreting that cystectomy or death will occur due to treatment, or incorrectly interpreting the timeframe in the levels as representing the time until the treatment starts to work (as opposed to the number of months until progression).
 - To aid interpretation for the upcoming DCE, wording updates to the description of the efficacy attribute were implemented following the interviews (see 'Updates to efficacy attribute wording' below).

Attribute importance

- Patients were asked about the importance of each attribute individually (i.e., not an indication of relative importance) (**Figure 2**).
 - All attributes tested were important to at least two-thirds of the sample (i.e., n≥8 patients per attribute).
 - Similar to the CE findings, *efficacy (event-free survival)* emerged as an important attribute for HR-NMIBC treatments.
 - Safety-related attributes were generally considered important, although flu-like symptoms was important to fewer patients relative to other safety attributes.

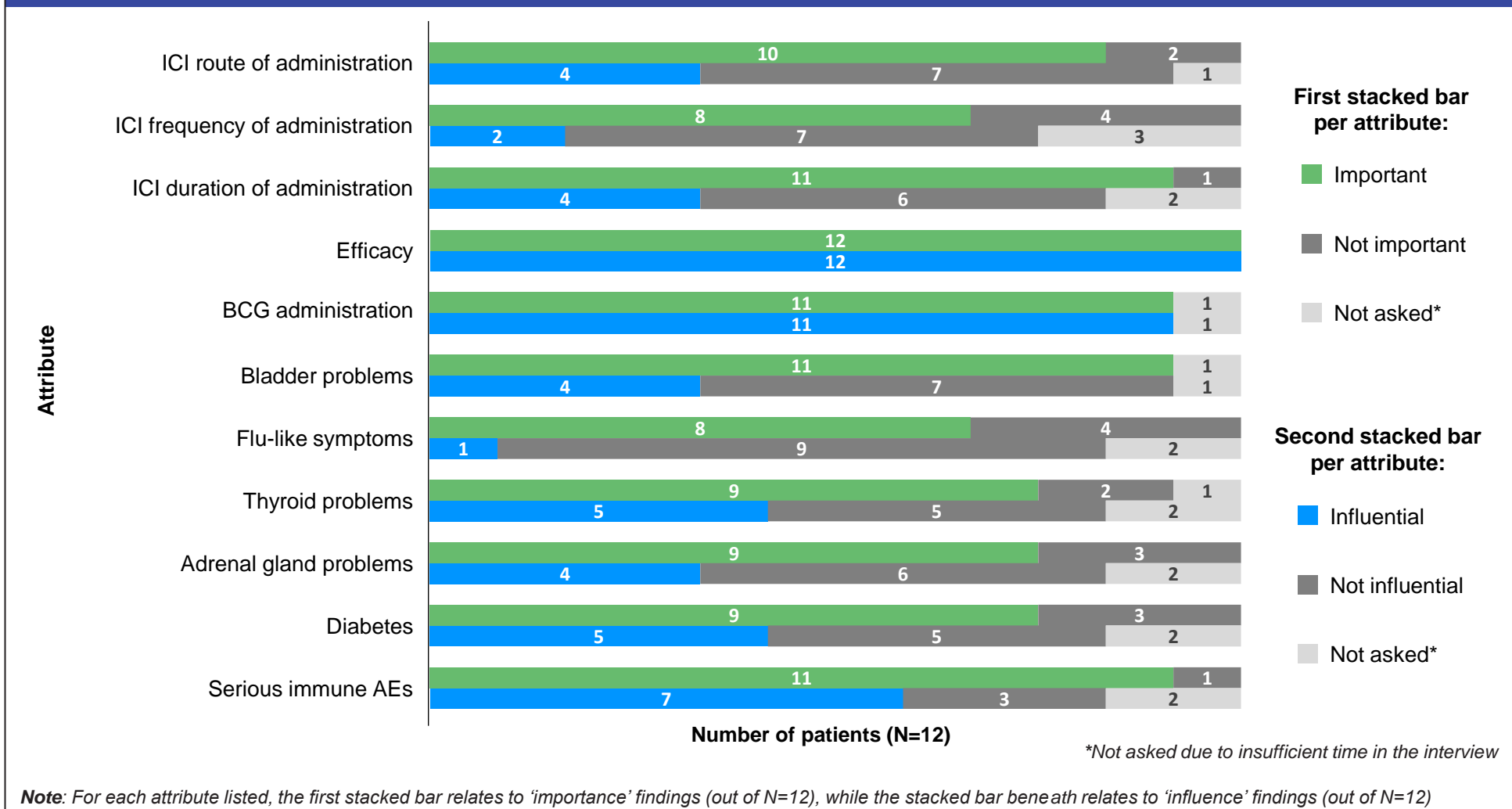


Perceived influence on treatment decision-making

- Serious immune AEs* attribute was considered to be influential by the majority of patients asked (n=7/10, 70.0%).
- When asked to discuss if attributes would impact the decision to take a treatment for HR-NMIBC, a number of attributes that had been previously discussed as being important did not emerge as influential in deciding whether to take a treatment (**Figure 2**).
 - Patients often re-iterated that an efficacious treatment is preferred, with side effects/administration being secondary.

"I'd be willing to go through something [flu-like symptoms] that made me sick for two or three days if it provided a better result than other types of treatment." (**Patient 3**)

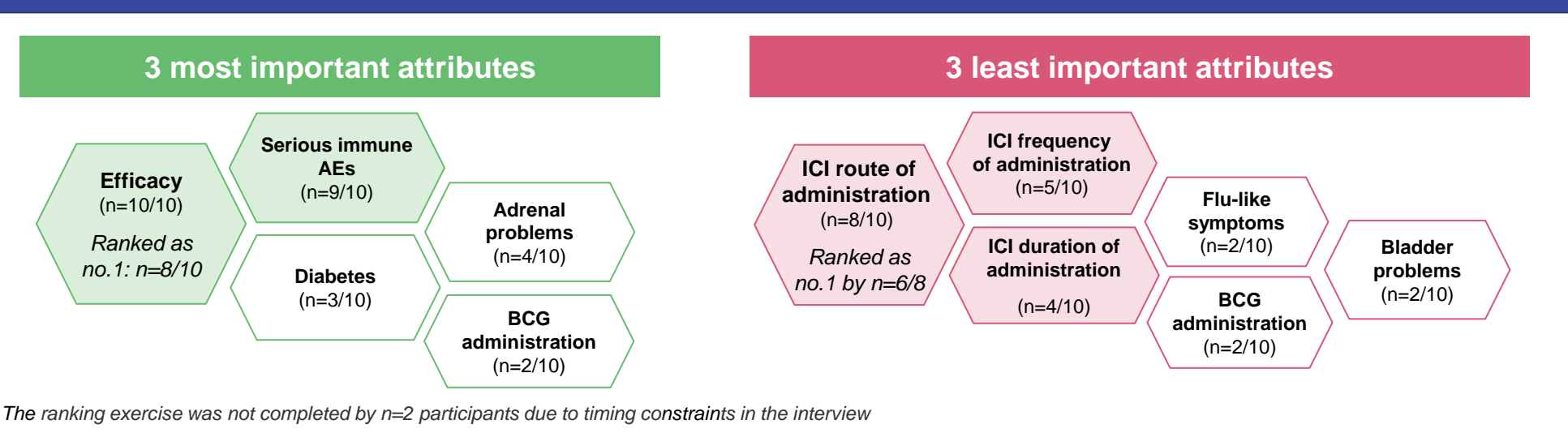
Figure 2. Patient-reported importance of each attribute and influence of each attribute on treatment choice



ATTRIBUTE RANKING TASK

- Patients were asked to list the 'three most important' and 'three least important' of the 11 attributes included in the original A&L grid, to provide a qualitative indication of the importance of attributes relative to each other (**Figure 3**).

Figure 3. Attributes in the original A&L grid ranked as the '3 most important' and the '3 least important' to patients



- Efficacy* and *serious/life-threatening AEs* (e.g., *serious immune AEs*, *adrenal problems*) were ranked as the top three most important attributes by the greatest number of patients, among attributes included in the draft A&L grid.
- Most patients ranked *ICI route of administration* as one of the least important attributes in the draft A&L grid.
 - Of note, during the CD questioning at the individual attribute level, patients discussed that the difference between a subcutaneous injection and an IV infusion was important; with most (n=10/11, 90.9%) discussing a preference for a subcutaneous injection.
 - ICI route of administration* was also the most frequently spontaneously mentioned attribute during CE section of the interviews.
- In contrast, *BCG administration* was ranked as one of the 3 most important attributes (n=2/10, 20.0%).
 - This may be due to intravesical administration being a more invasive/pressing concern than a subcutaneous injection or an IV infusion. Patients in this study had received BCG before but had not received an ICI therapy previously.
 - At the patient-level, the attributes ranked among the 'three least important' were largely supported by the CD findings, with those same participants reporting the attributes as not being influential to treatment decisions.
 - However, some attributes were generally considered to be important when asked in the CD; highlighting that participants may respond differently when asked to consider the importance of different attributes in relation to each other (**Figure 2**).

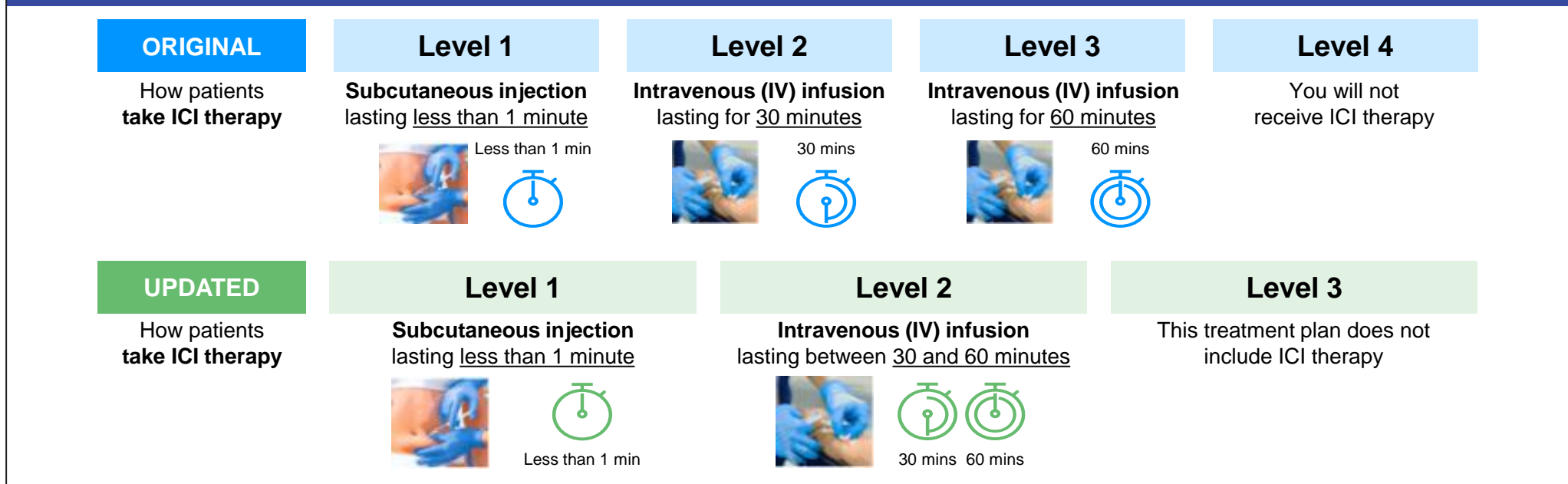
Attribute rating task (0-10 numerical rating scale [NRS])

- Efficacy*, *serious immune side effects*, and long-term side effects (*diabetes and adrenal gland problems*) were rated as highly important with most patients providing a rating of ≥7 on a 0-10 NRS.
- Flu-like symptoms*, *ICI frequency* and *ICI route of administration* were rated as less important, with most patients providing a rating of ≤4 on a 0-10 NRS.
- Several attributes (particularly administration attributes) were rated as either *very high* or *very low* importance across the sample, indicating differences in perspectives among the sample and potential preference heterogeneity.
- Findings are generally consistent with attribute importance ratings (**Figure 2**) and rankings (**Figure 3**) and provide additional insights into the magnitude of importance per attribute.

LEVEL FINDINGS AND UPDATES

- For attributes selected for inclusion in the DCE, qualitative evidence supported the extent to which minimum and maximum levels of these attributes encompassed a salient and sufficiently testable range.
- Attributes for which the range of levels did not represent meaningful differences were removed from the A&L grid (i.e., adrenal gland problems, flu-like symptoms).
 - None of the patients had expressed that the ranges of the levels were unreasonably or unrealistically large.
- Differences in levels within the attributes selected for inclusion were perceived as being meaningfully different, supporting mutual exclusivity.
 - For the *ICI route of administration* attribute, the levels representing IV for 30-minutes and IV for 60-minutes were combined following feedback that most patients (n=7/11, 63.6%) did not consider this difference to be meaningful (**Figure 4**).

Figure 4. Updates made to ICI route of administration levels

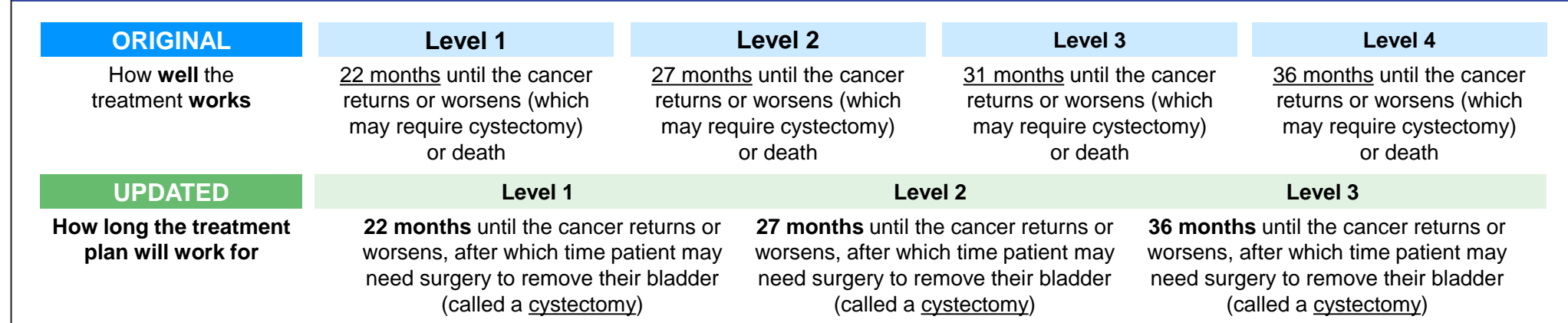


UPDATES TO ATTRIBUTE WORDING

Efficacy attribute

- Attribute wording was updated to improve clarity, aid comprehension, and improve patient-friendliness.
 - This involved avoiding complex clinical terminology (e.g., "surgery to remove the bladder" to further describe "cystectomy") and the reframing of attribute wording to clearly describe *how long the treatment works* (shown in **Figure 5**) to better align with the endpoint definition of event-free survival.
- Qualitative findings indicated that *efficacy* may be a dominant attribute in decision-making.
 - The attribute wording was revised to remove mention of 'death'. This attribute originally included 'death' to align with endpoint definitions of event-free survival; however, input from an expert urologist and a patient advocate highlighted how death is not typically a central focus in patient-clinician discussions at this stage of the disease. Instead, these discussions focus primarily on disease progression and treatment burden.

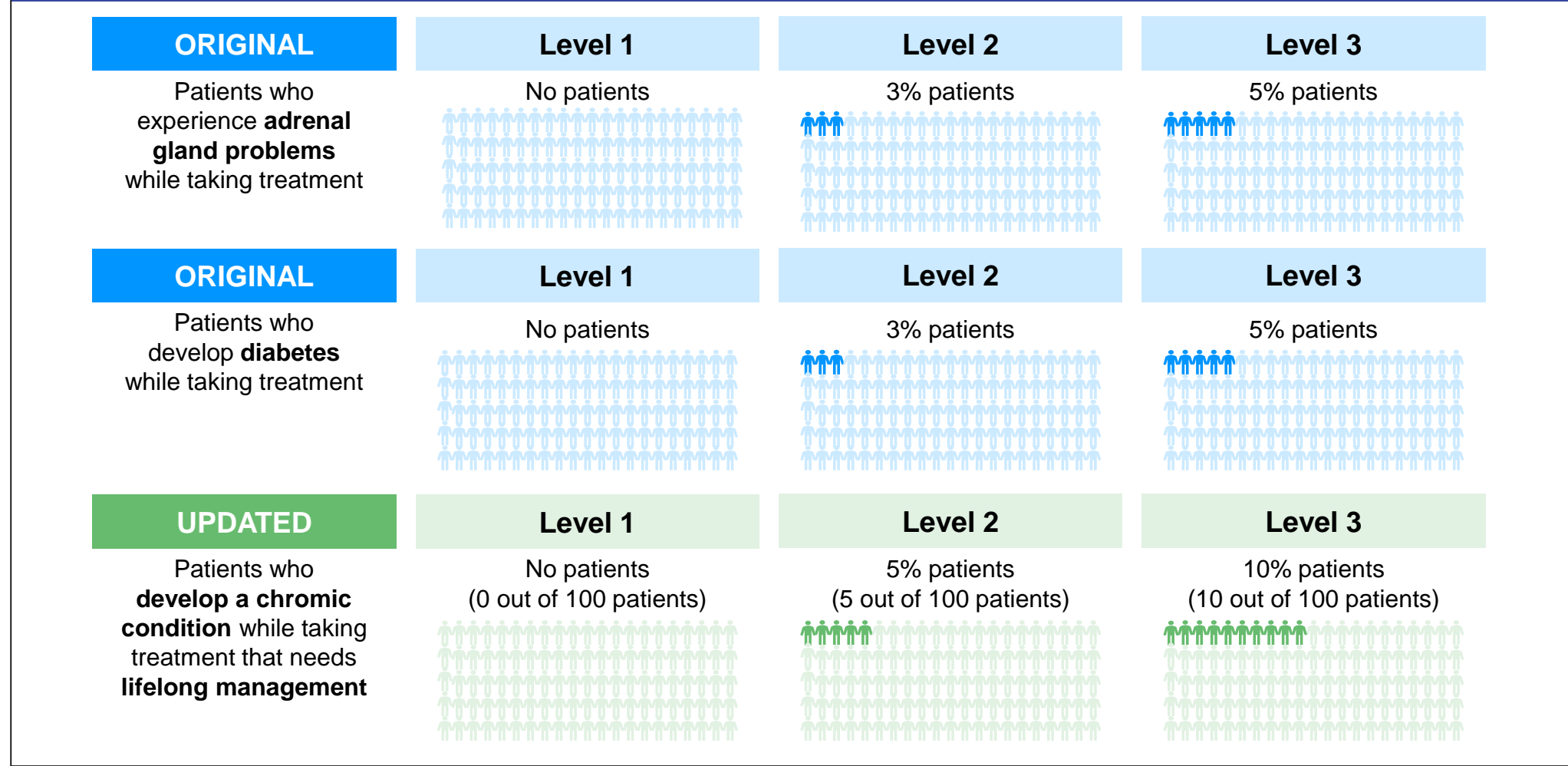
Figure 5. Updates made to efficacy attribute wording



Developing a combined attribute for endocrine-related conditions

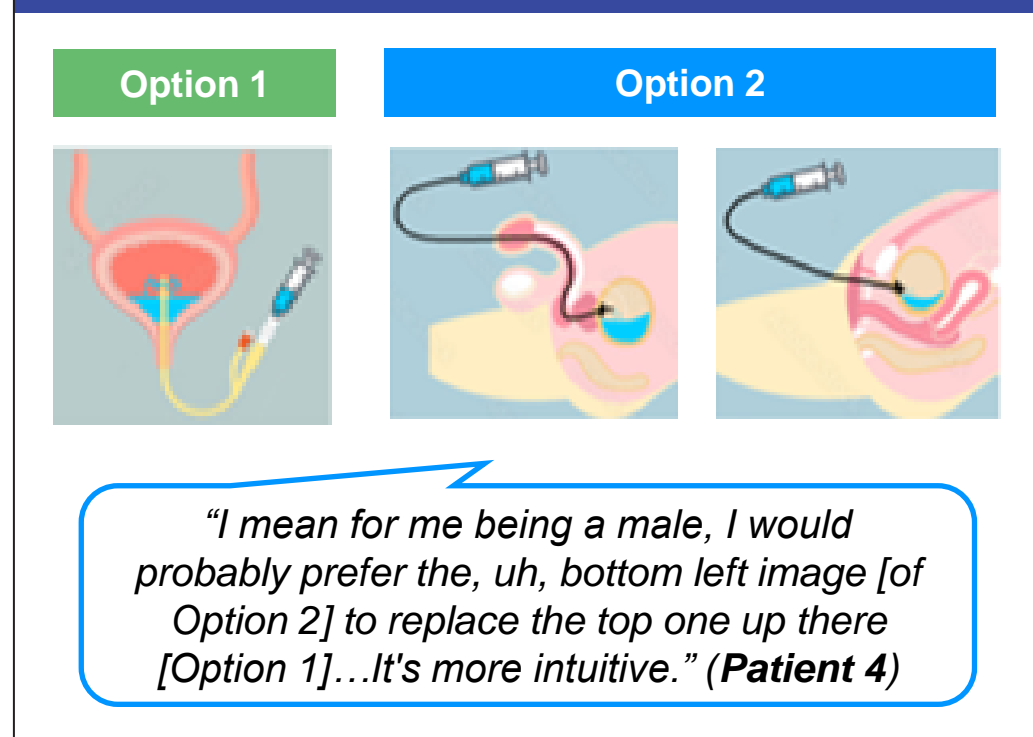
- When discussing *diabetes* and *adrenal gland problems*, patients often discussed how the most important/consequential factor was the need to take lifelong treatment (injections, pills, or supplements) to manage these chronic conditions.
- Diabetes* and *adrenal gland problems* were combined given similarities between these attributes (i.e., both being endocrine-related, chronic conditions) and the wording was re-framed to emphasize the implications of life-long disease management (**Figure 5**).

Figure 6. Updates made to chronic endocrine-related attributes



UPDATES TO SUPPLEMENTARY IMAGES

Figure 7. Updates made to the BCG administration images



"I mean for me being a male, I would probably prefer the, uh, bottom left image [of Option 2] to replace the top one up there [Option 1]...It's more intuitive." (**Patient 4**)

BCG administration attribute

- In the interviews, patients were presented with two sets of images intended to illustrate BCG intravesical instillation (**Figure 7**).
 - Most patients (n=4/7, 57.1%) expressed that they preferred *Option 2* to *Option 1*.

ATTRIBUTES REMOVED FROM THE A&L GRID

- It is necessary to limit the number of attributes included in a full-profile DCE to minimize cognitive burden and ensure that respondents are able to consider all attributes when completing the choice tasks.
- Based on the qualitative interviews, three attributes were removed from the A&L grid.

- Collectively, the attributes removed were either not considered by patients to be influential to treatment decisions, were of low importance (as indicated via rating and ranking task responses), and/or included no meaningful differences in levels (**Table 2**).
- Attribute selection and removal was informed by striking a balance between patient feedback, alongside expert clinical input, considerations regarding the expected decision-making context, and the specific research question.
- Appreciable methodological considerations were also considered (e.g., a need to refine the number of attributes and levels for the planned DCE experimental design).
- Final attribute selection also ensured that attributes representing key categories regarding treatment options were adequately represented within such a study design (i.e., administration, efficacy, and safety profile).

Table 2. Attributes removed from the A&L grid

ICI duration of administration	The duration of ICI therapy was not considered to be key information that is routinely discussed (or appropriate to discuss) in patient-clinician decisions regarding ICI therapies, due to inherent differences between trial design procedures and real-world, in-practice prescribing.
Flu-like symptoms	This attribute was not considered to be influential to treatment decision-making by a substantial proportion of the sample (primarily based on the incidence range). This finding was substantiated when observing how important other BCG-related AEs (i.e., bladder problems) were to patients.
Thyroid disorders	Among the other endocrine-related attributes tested (i.e., adrenal insufficiency, diabetes), this attribute was not highlighted as a key attribute of importance or influence to treatment decisions.