Rapid Review: Were there any clinical trials in non-muscle invasive bladder cancer that naturally adopted the updated FDA COA oncology guidance?

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Background & Objectives

- In June 2021, the Food and Drug Administration (FDA) released updated guidelines on core patient-reported outcomes (PROs) in **cancer clinical trials** (FDA, 2021). The guidelines (specific to registration trials for anti-cancer therapies intended to demonstrate an effect on survival, tumor response, or delay in the progression of a malignancy) emphasized the need to focus on five **patient-reported** concepts:

1) 'Disease related symptoms'
2) 'Symptomatic adverse events (SAEs)'
3) 'Overall side effect impact'
4) 'Physical function'
5) 'Role function'

- The rationale was to facilitate a better understanding of treatment benefits by including patient reports. **Non-muscle invasive bladder cancer (NMIBC)** and associated treatments, have been found to impair quality of life (QoL) including physical and role functioning (Jung et al., 2019).
- This research aims to explore the extent to which clinical trials in NMIBC, that included QoL assessments, naturally covered the concepts outlined in the guidance before its publication.

Methods

- The following terms were used in PubMed: 'non-muscle invasive' AND 'cancer' AND 'bladder' AND ('quality of life' or 'PRO' or 'questionnaire') AND 'clinical' and 'trial'. Studies published in English describing NMIBC trials and including QoL assessments were identified and examined. As per the guidelines, 'overall side effect impact' was defined as the overall treatment side effect reported by patients (e.g. GP5 question of from the Functional Assessment of Chronic Illness Therapy (FACIT) item library); 'physical function' referred to the ability to perform activities that required physical effort (e.g. EORTC Quality of Life of Cancer Patients QLQ-C30-physical function scale) and 'role function' was defined as the impact of treatment on the ability to work and carry out daily activities (e.g. EORTC QLQ-C30 - role function scale) (FDA, 2021).

Results

- Out of the 20 studies resulting from the PubMed search on Jan 6th, 2022, **11 studies met the inclusion criteria.**
- The five concepts recommended *by* the FDA were partially covered and to a varying degree by a plethora of PROMs (e.g., EORTC QLQ-C30 - quality of life of cancer patients , BCI - bladder cancer index).
- Patient-reported assessment of disease symptoms, physical and role function were assessed in all studies. Overall side effect impact was examined by 2 of 11 studies while patient-reported symptomatic AEs were not assessed in any.

Conclusions

- While the majority of PRO concepts recommended by the FDA were assessed in the trials, there was a lack of emphasis on the patient perspective of adverse events and their impact on the patient.
- The adoption of the FDA guidelines across all NMIBC clinical trials as well as a standardized approach to assessing these, could improve understanding of the impact of therapies on patients and allow for a more comprehensive analysis of risk/benefits of cancer treatments.

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	Trial phase	Main concept measured	PRO concepts				
			1)	2)	3)	4)	5)
Colombo, Rocchini, Suardi et al., (2012)	II	-Symptoms -QoL (SF-36) -Response to treatment	☑	☒	☒	☑	☑
Hayne, Stockler, McCombie et al., (2015)	III	-Symptom recurrence -Progression -QoL (EORTC QLQBLS-24, EORTC QLQ-C30, IPSS) -Prognosis/survival	☑	☒	☒	☑	☑
Khan, Gan, Ahmed et al., (2016)	I	-Symptoms -Prognosis -QoL (FACT-Bl, FACT-G)	☑	☒	☑	☑	☑
Oughton, Poad, Twiddy et al., (2017)	III	-QoL (EQ-5D, EORTC QLQ-C30, EORTC QLQ-BLM30, EORTC QLQ-NMIBC24) -Symptom recurrence	☑	☒	☒	☑	☑
Tan, Panchal, Buckley et al., (2019)	III	-Survival time -QoL (EQ-5D) -Disease progression	☑	☒	☒	☑	☑
Kelly, Tan, Porta et al., (2019)	III	-Symptoms recurrence -QoL (EORTC QLQ-BLS24, EORTC QLQ-C30)	☑	☒	☒	☑	☑
Ji, Mukherjee, Reyes et al., (2019)	I	-Response to treatment -QoL - Symptoms and Functionality (AUASS, BCI)	☑	☒	☒	☑	☑
Mostafid Porta, Cresswell et al., (2020)	II	-QoL (EORTC QLQ-C30, EORTC QLQ-NMIBC24) -Response to treatment -Symptom recurrence	☑	☒	☒	☑	☑
Mastroianni, Tuderti, Anceschi et al., (2021)	S.	QoL (EORTC QLQ-BLM30) -Functionality -Survival	☑	☒	☒	☑	☑
Arthuso, Fairey, Boulé et al., (2021)	II	QoL (EORTC QLQ-C30, EORTC QLQ-NMIBC24) -Symptoms -Exercise intervention	☑	☒	☒	☑	☑
Miyake, Nishimura, Inoue, et al, (2021)	III	-Symptoms -Prognosis -HR-QoL (SF-8, EORTC QLQ-C30, FACT-BL, IPSS, OABSS)	☑	☒	☑	☑	☑

1) Disease related symptoms; 2) Symptomatic adverse events (SAEs); 3) Overall side effect impact; 4) Physical function; 5) Role function.

S: Superiority trial; AEs: Adverse events; QoL: quality of life; HR-QoL: Health-related quality of life; IPSS: International Prostate Symptom Score; OABSS: overactive bladder symptom score; BCI: bladder cancer index; AUASS: American Urologic Association Symptom Score; SF: short form survey; EORTC: European Organization for Research and Treatment of Cancer.