Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000117: Network/Function Assessment of Cancer Therapy-Disease Related Symptom Scale (NFKSI-DRS)
Letter of Intent

Administrative Structure:

Description of the submitter including, but not limited to, principal investigator(s), working group member(s), institutions, and contact information not contained within the cover letter.

This proposal is being submitted by FACIT.org through Northwestern University.

The initial development work for the measure being proposed for entry into the qualification program was funded by grants from the following pharmaceutical companies: Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb, Centocor, Cell Therapeutics, Inc., Genentech, GlaxoSmithKline, Eli Lilly and Company, Merck & Co., Novartis, Ortho Biotech, Pfizer, Sanofi-Aventis, and Takeda Pharmaceuticals.

The lead contact for this application is David Cella, PhD.

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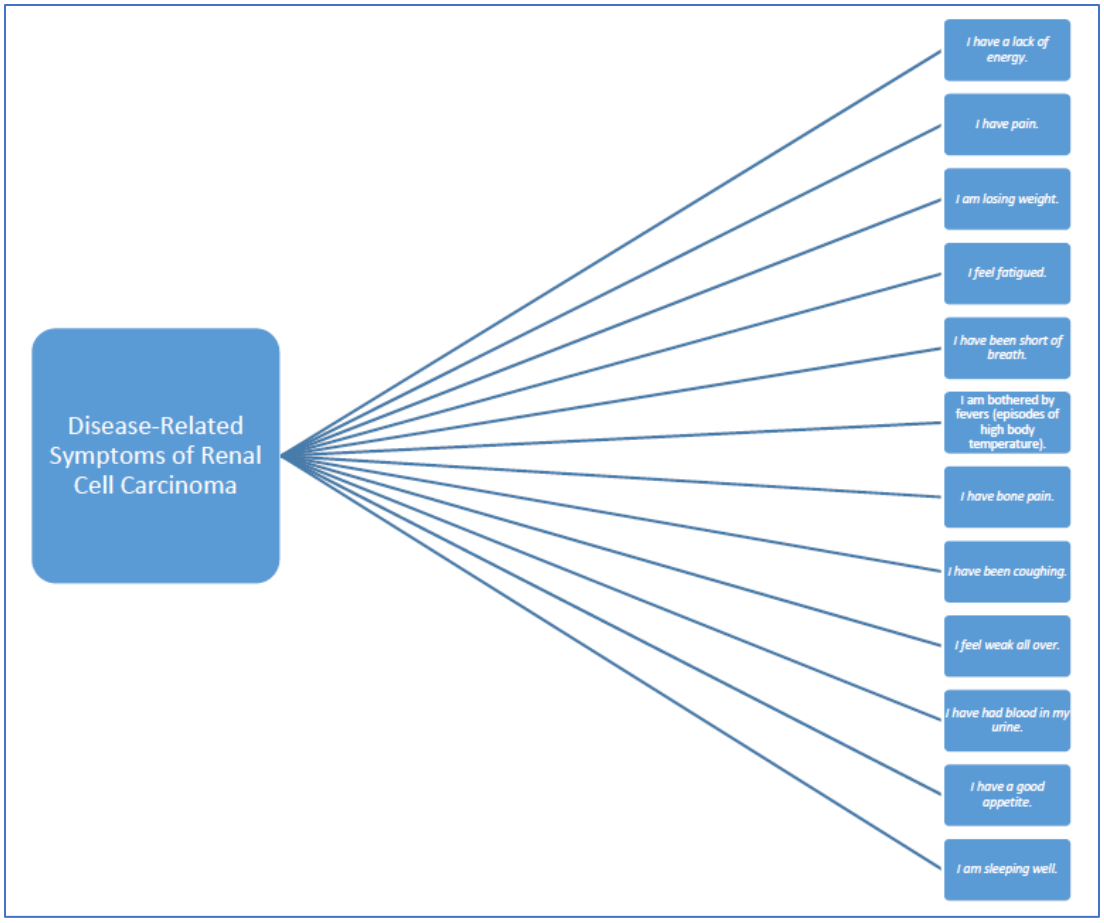
Concept(s) of Interest (COI) for Meaningful Treatment Benefit:

A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

The concepts of interest for the PRO measure are disease-related symptoms of renal cell carcinoma, as measured by the 12 physical items of the 13-item NFKSI-Disease Related Symptom Scale (NFKSI-DRS).

Provide a conceptual framework for the COA(s)

Below is the hypothesized conceptual framework for the 12-item NFKSI-DRS-Physical (NFKSI-DRS-P)



Context of Use for COA Qualification:

Targeted study population including a definition of the disease and selection criteria for clinical trials (e.g., baseline symptom severity, patient demographics, comorbidities, language/culture groups).

The NFKSI-DRS-P is intended to assess changes in disease-related symptoms for adults with advanced or metastatic renal cell carcinoma.

The target population includes patients aged 18 years or older, with histological confirmation of renal cell carcinoma (RCC) with a clear-cell component, diagnosed with advanced (not amenable to curative surgery or radiation therapy) or metastatic (AJCC Stage IV) RCC. Target population patients will also have measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, have adequate organ function, based on standard laboratory tests, and a Karnofsky Performance Status (KPS) of at least 70%.

Targeted study design and statistical analysis plan (includes the role of the planned COA in future drug development clinical trials, including the planned set of primary and secondary endpoints with hierarchy, if appropriate).

The scores resulting from the proposed PRO measure will be positioned as a key endpoints in future renal cell carcinoma (RCC) treatment trials. It is expected that the resulting endpoint (change in RCC

disease-related symptoms), as measured by the NKFSI-DRS-P may be used as a primary or co-primary endpoint to establish treatment benefit or as a secondary endpoint to support labeling claims from data produced in randomized controlled clinical trials where an experimental treatment for RCC is being tested. Comparisons can be made to both placebo groups and comparator drug groups depending on the number of arms in the clinical trial. The specific endpoint selection, positioning, and measurement approach would be determined by the study sponsor in concert with the appropriate regulatory review agencies.

A study statistical analysis plan for an existing RCC treatment trial will be developed, but has not yet been identified at this time. This plan will outline appropriate tests to assess various psychometric properties of the measure of RCC disease-related symptoms, including (but not limited to) concurrent validity, responsiveness to changes, and treatment response.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***

The NFKSI-DRS-P has been translated for use outside the U.S. and are intended for use in multinational trials or trials within a single country where multiple language and cultural groups may be enrolled. The NFKSI DRS-P scale was developed originally in English and has since been translated into the following languages: Arabic, Bosnian, Chinese (simplified), Chinese (traditional), Croatian, Czech, Danish, Dutch, Estonian, Finnish, French, German, Greek, Hindi, Hebrew, Hungarian, Italian, Japanese, Korean, Malay, Norwegian, Polish, Portuguese, Romanian, Russian, Serbian, Slovak, Spanish, Swedish, Tamil, Thai, Turkish, Ukranian, and Vietnamese.

- ***Other study setting specifics (e.g., inpatient versus outpatient)***

The target population is adult patients with advanced or metastatic RCC.

COA Type: PRO