INPLASY PROTOCOL

Corresponding author:
Heather Jim

heather.jim@moffitt.org

Author Affiliation:
Moffitt Cancer Center

Review Stage at time of this submission: Data analysis.

Conflicts of interest:
Gonzalez, B: SureMed Compliance, Elly Health. Dicker, A: Advisory activities Roche, EMD Serono, Celldex, Janssen, Cybrexa, SelfCare Catalysts, OncoHost, Thirdbridge, Noxopharm, Varian, Accordant, Moleculin. Jim, H: Consultant for RedHill BioPharma, Janssen Scientific Affairs, Merck

Protocol: Meta-Analysis of Quality of Life in Cancer Patients Treated with Immune Checkpoint Inhibitors

Gonzalez, B[1]; Eisel, S[2]; Bowles, K[3]; Hoogland, A[4]; James, B[5]; Small, B[6]; Sharpe, S[7]; Hyland, K[8]; Bulls, H[9]; Christy, S[10]; Mansfield, J[11]; Nelson, A[12]; Alla, R[13]; Maharaj, K[14]; Kennedy, B[15]; Lafranchise, E[16]; Williams, N[17]; Jennewein, S[18]; Postow, M[19]; Dicker, A[20]; Jim, H[21].

Review question / Objective: P = Adult cancer patients I = Immune checkpoint inhibitors administered (alemtuzumab, nivolumab, pembrolizumab, pidilizumab, BMS 936559, durvalumab, Atezolizumab, Avelumab, Ipilimumab, Tremelimumab, rituximab, ofatumumab) C = N/A O = Primary outcome: PRO (patient-reported outcome) Secondary outcome: Quality of Life (wellness, wellbeing, QoL, etc.) S = Original data (not a review, meta-analysis, secondary data analysis, case report, case series, commentary, retrospective, registry studies, etc...). Clinical Trials, Randomized Control Trials, etc. Expanded access trials are acceptable.

Rationale: Clinical trials of immune checkpoint inhibitors (ICIs) have published patient-reported quality of life (QOL). The size and heterogeneity of this literature can make patient education difficult. The aim of this meta-analysis is to describe summarize QOL in patients receiving ICIs for cancer.

Condition being studied: Cancer being treated with a PD-1/PD-L1 and/or CTLA-4 inhibitor.

INTRODUCTION

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METHODS

Search strategy: The following databases will be searched: PubMed, EMBASE, Web of Science. In addition, a secondary hand search of conference abstracts will be conducted from relevant scientific societies.

Participant or population: Cancer patients being treated with a PD-1/PD-L1 and/or CTLA-4 inhibitor and comparison groups.

Intervention: PD-1/PD-L1 and/or CTLA-4 inhibitor.

Comparator: various (e.g., chemotherapy, placebo, investigator's choice).

Study designs to be included: prospective, longitudinal, observational or interventional designs.

Eligibility criteria: 1. Consist of a sample exclusively composed of cancer patients (any diagnosis or disease stage) 2. All or a subset of study participants treated with an immune checkpoint inhibitor (i.e., atezolizumab, avelumab, BMS 936559, durvalumab, ipilimumab, nivolumab,

pembrolizumab, pidilizumab, ticilimumab, or tremelimumab) 3. Report original data, which may include expanded access data 4. All study participants are adults (i.e., at least 18 years old) 5. Patient-reported quality of life data reported 6. Prospective, longitudinal study design 7. Observational or interventional design 8. Peer-reviewed paper or conference abstract.

Information sources: The following databases will be searched: PubMed, EMBASE, Web of Science. In addition, a secondary hand search of conference abstracts will be conducted from relevant scientific societies. When there is not sufficient information to calculate effect sizes, study authors and/or sponsors will be contacted.

Main outcome(s): Overall quality of life.

Data management: Data will be independently extracted and checked by rater pairs using Covidence software. Discrepancies in study selection and data extraction will be resolved by senior authors. Information to be extracted includes QOL data (i.e., means, standard deviations, 95% confidence intervals, sample size), study design characteristics (i.e., disease site, ICI regimen, comparison regimen, timing of assessments), and sample characteristics (i.e., mean age, percent female).

Quality assessment / Risk of bias analysis: Two reviewers will independently rate each study selected for inclusion using the Cochrane Risk of Bias Assessment criteria. The reviewers' ratings will be based upon information found in the PRO publication or other study publications, including appendices and supplemental materials (e.g., study protocol) when available. Discordant ratings will be discussed by the reviewers and consensus reached on a final, overall rating (i.e., high versus low risk of bias).

Strategy of data synthesis: Two meta-analyses will be conducted. One will examine change in QOL in patients treated with ICIs from pre-treatment baseline to

follow-up. The second will compare QOL at follow-up in ICIs versus non-ICI regimens.

Subgroup analysis: Meta-analyses will be grouped by ICI regimen. Meta-regression analyses will be conducted using random-effects models to examine study level moderators of effect size. It is anticipated that these will include type of ICI regimen, type of comparison regimen, disease site, mean sample age, sample gender composition, and risk of bias.

Sensibility analysis: Funnel plots and trim and fill will be used to assess publication bias for both meta-analyses.

Language: No language limits.

Country(ies) involved: Authors are based in the United States. Data from any country will be included if the study meets inclusion criteria.

Keywords: Antineoplastic agents, immunological; neoplasms; quality of life; patient reported outcome measures.

Dissemination plans: Findings will be submitted for publication in a peer-reviewed journal.

Contributions of each author:
Author 1 - Brian Gonzalez - literature search, figures, study design, data collection, data analysis, data interpretation, writing.
Author 2 - Sarah Eisel - literature search, figures, data collection, data analysis, data interpretation, writing.
Author 3 - Kristine Bowles - literature search, figures, data collection, data analysis, writing.
Author 4 - Aasha Hoogland - literature search, data collection, data analysis, writing.
Author 5 - Brian James - literature search, data collection, writing.
Author 6 - Brent Small - data collection, data analysis, data interpretation, writing.
Author 7 - Susan Sharpe - literature search, writing.
Author 8 - Kelly Hyland - literature search, data collection, writing.

Author 9 - Hailey Bulls - literature search, data collection, writing.
Author 10 - Shannon Christy - literature search, data collection, writing.
Author 11 - Jori Mansfield - literature search, data collection, writing.
Author 12 - Ashley Nelson - literature search, data collection, writing.
Author 13 - Raviteja Alla - literature search, data collection, writing.
Author 14 - Kelly Maharaj - literature search, data collection, writing.
Author 15 - Brittany Kennedy - literature search, data collection, writing.
Author 16 - Elizabeth Lafranchise - literature search, data collection, writing.
Author 17 - Noelle Williams - literature search, data collection, writing.
Author 18 - Sarah Jennewein - literature search, data collection, writing.
Author 19 - Michael Postow - study design, writing.
Author 20 - Adam Dicker - study design, writing.
Author 21 - Heather Jim - literature search, figures, study design, data collection, data analysis, data interpretation, writing.