SUPPORTING INFORMATION

The studies from the current review were identified from the National Institutes of Health clinicaltrials.gov database and the World Health Organization International Glinical Trials Registry Platform using the following search terms: "heavy charged particles", "carbon", "heavy particle therapy", and "carbon radiotherapy". Searches were conducted by two of the authors (AL, RS) and search results were independently reviewed by a third author (MR) to ensure that GIRT clinical trials met the inclusion/exclusion criteria described below.

All the clinical trials identified in these databases as of July 16, 2017 were included in this review. Trials were eligible if they were reported in clinicaltrials.gov or WHO 2004 onward, included GIRT alone, or were comparative trials with GIRT. Studies were listed as described in the clinicaltrials.gov database, including "completed", status "unknown", or stopped before completion denoted as "terminated". Observational studies were not included when the subjects in the cohort were described as receiving "diagnostic or therapeutic interventions, but the investigator does not assign specific interventions to the subjects of the study". This definition is consistent with the updated National Institutes of Health definition of a clinical trial, as described at grants.nih.gov.

We extracted the following data from each clinical trial meeting the inclusion criteria: age group (pediatric, adult, or both), number of patients enrolled (planned or after completion), enrollment status (completed, no longer recruiting, not yet recruiting,

recruiting, results reported, terminated, unknown), enrollment start date included expected enrollment date, phase (I, I/II, II, or III), country of origin, disease site(s), intervention radiation (e.g. carbon ion only, carbon ions vs. protons, carbon ions vs. photons, and allocation type) and random vs. non-random allocation. Each clinical trial was classified into one of the following disease sites: base of skull, bone, bone and soft tissue, breast, cervix, central nervous system (GNS), esophagus, head and neck (H&N), kidney, liver, lung, pancreas, prostate, rectum, sacrum, and multiple sites (if two or more sites were listed). The tumor-control or survival-related endpoints were classified as local control (LG), overall survival (OS), progression free survival (PFS), including local PFS and recurrence-free survival (RFS). Survival related endpoints included treatment-related toxicity, other adverse advents, and maximum tolerated dose (MTD), i.e., endpoints typically assessed in phase I trials or the phase I component of phase I/II trials. Descriptive statistics (e.g., frequencies and percentages for categorical variables and medians for variables measured on a continuous scale) were used to describe trial characteristics. Due to rounding, total percentages can exceed 100%.