Appendix Table C7. Description of studies that address Key Question 2

| Study | Study design, enrollment numbers and lost to FU/excluded | Inclusion/exclusion criteria | Stage Distribution | Tumor/Obstruction Location & Histopathology | Patient characteristics |
| --- | --- | --- | --- | --- | --- |
| Chen-2012,  USA, #4554 | **Study design:**  PRO, SAS  **Patients enrolled:**  40 (100%)  **Lost to FU/excluded/missing:**  0 | **Inclusion criteria:**  1. Hst confirmed, primary clinical stage I NSCLC  2. Medically operable, high risk  **Exclusion criteria:**  Inability to safely implant  fiducials for tumor tracking | **Stage I:** 40 (100%) | **Location:**  NR  **Histopathology:**  Hst confirmed: 40 (100%)  ACC: 19 (48%)  SCC: 12 (30%)  NSCLC NOS: 9 (22%) | **Age (years):**  Median 76 (63-87)    **Women:**  24 (60%)  **Race:**  Caucasian  33 (82%)  **Co-morbidities:**  Mean DLCO  10 (3.5-23.3 mL/min/mm  Hg)  Predicted mean DLCO  55% (14-128%)  Predicted mean FEV1  57% (21-111%)  **Current or former**  **smoker:** 38 (95%)  **Performance status:**  Median ECOG  1 (0-2) |
| Iwata-2010, Japan, # 1747 | **Study design:**  NRCS, NR whether data collection was RET or PRO  **Patients enrolled:**  Total: 57 (100%)  PBRT 80Gy: 20 (35%)  PBRT 60 Gy: 37 (65%)  Refusal:  Total: 28 (100%)  PBRT 80Gy: 10 (34%)  PBRT 60 Gy: 18 (64%)  **Lost to FU/excluded/missing:**  None | **Inclusion criteria:**   1. Hst confirmed primary NSCLC staged IA or IB (International Union Against Cancer 2002 staging system) 2. Medically inoperable or refused surgical resection 3. WHO performance status ≤2 4. No history of previous LC 5. No prior chest RT or chemotherapy;   **Exclusion criteria:**  NR | Total: 57 (100%)  Stage 1A: 27(47%)  Stage 1B: 30 (57%)  PBRT 80Gy: 20 (100%)  Stage 1A: 6 (30%)  Stage 1B: 14(70%)  PBRT 60 Gy: 37 (100%)  Stage 1A: 21 (57%)  Stage 1B: 16 (43%) | **Location:**  NR  **Histopathology:**  Total: 57 (100%)  AC: 32 (56%)  SCC: 23 (40%)  Others: 2 (4%)  PBRT 80Gy: 20 (100%)  AC: 11 (55%)  SCC: 8 (40%)  Others: 1 (5%)  PBRT 60 Gy: 37 (100%)  AC: 21 (57%)  SCC: 15 (41%)  Others: 1 (3%) | **Age:**  Total: 76 (48-89)  PBRT 80Gy: 75 (48-87)  PBRT 60 Gy: 78 (57-87)  **Women:**  Total: 23 (29%)  PBRT 80Gy: 7 (36%)  PBRT 60 Gy: 7 (19%)  **Race:**  NR  **Co-morbidities:**  Total: 28 (100%)  Pulmonary: 13 (46%)  CVD: 9 (32%)  Severe DM: 5 (18%)  Age: 2 (7%)  Others: 2 (7%)  PBRT 80Gy: 10 (100%)  Pulmonary: 7 (70%)  CVD: 3 (30%)  Severe DM: 1 (10%)  Age: 0  Others: 0  PBRT 60 Gy: 18 (100%)  Pulmonary: 6 (33%)  CVD: 6 (33%)  Severe DM: 4 (22%)  Age: 2 (11%)  Others: 2 (11%)  **Performance status:**  NR |
| Lagerwaard-  2011,  Netherlands,  #2122 | **Study design:**  RET, SAS  **Patients enrolled:**  177 (100%)  **Lost to FU/excluded/missing:**  0 | **Inclusion criteria:**  1. Primary clinical stage I NSCLC  2. Medically operable  **Exclusion criteria:**  1. GOLD COPD class 3-4  2. FEV1 < 50% of predicted  3. DLCO < 50% of predicted  4. WHO performance status ≥ 3  5. Major comorbidity (cardiac, renal) that precludes surgery | **Stage I:** 177 (100%) | **Location:**  NR  **Histopathology:**  Hst confirmed: 60 (33%)  ACC: 20 (33%)  SCC: 16 (27%)  NSCLC NOS: 24 (38%)  Undiagnosed: 117 (66%) | **Age (years):**  76 (50-91)    **Women:**  76 (43%)  **Race:**  NR  **Co-morbidities:**  GOLD COPD  No COPD: 65 (37%)  Class I: 37 (21%)  Class II: 75 (42%)  **CCI score:**  0: 18 (10%)  1: 59 (33%)  2: 38 (22%)  3: 39 (22%)  4: 16 (9%)  5: 7 (4%)  **Current or former**  **smoker:** 168 (95%)  **Performance status:**  WHO < 3: 177 (100%) |
| Onishi-2011,  Japan, #2802  (longer FU to  Onishi-2007,  Japan, #2803) | **Study design:**  RET, SAS  **Patients enrolled:**  87 (100%)    **Lost to FU/excluded/missing:**  0 | **Inclusion criteria:**  1. Hst confirmed primary clinical stage I NSCLC  2. Medically operable but refused surgery  **Exclusion criteria:**  NR | Stage I: 87 (100%) | **Location:**  NR  **Histopathology:**  Hst confirmed: 87 (100%)  ACC: 54 (62%)  SCC: 25 (29%)  NSCLC NOS: 8 (9%) | **Age (years):**  74 (43-87)    **Women:**  24 (28%)  **Race:**  NR  **Co-morbidities:**  Chronic lung disease: 38  (44%)  **Performance status:**  ECOG  0: 51 (59%)  1: 30 (34%)  2: (7%) |
| Shibamoto 2012,  Japan, #4629 | **Study design:**  PRO, SAS  **Patients enrolled:**  Total: 180 (100%)  Medically inoperable: 120 (67%)  Refused surgery: 60 (33%)  **Lost to FU/excluded/missing:**  0 | **Inclusion criteria:**  Histologically proven  NSCLC stage 1 not  suitable for surgery for  medical or functional  reasons  **Exclusion criteria:**   1. Tumor > 5 cm in greatest dimension 2. WHO PS < 2 or PS 3 when not due to pulmonary   disease   1. Active concurrent cancer 2. FEV1/FVC < 60% or percentage vital capacity < 75% | **Stage I:** 180(100%) | **Location:**  Not stated by operability  **Histopathology:**  Pathological confirmation:  180 (100%)  Not stated by operability | **Age (years):**  77 (29-89) all cases  **Women:**  57 (32%) all cases  **Race:**  NR  **Comorbidities:**  NR  **Performance status:**  WHO  0: 87 (48%)  1: 69 (38%)  2: 21 (12%)  3: 3 (2%)  all cases |
| Takeda-2009,  Japan, #3700 | **Study design:**  RET, SAS  **Patients enrolled:**  Total: 63 (100%)  Medically inoperable: 49 (78%)  Operable: 14 (22%)    **Lost to FU/excluded/missing:**  0 | **Inclusion criteria:**  1. Primary clinical stage I  NSCLC  2. WHO performance status  ≤ 2  **Exclusion criteria:**  1. Prior radiation to lung or mediastinum | Stage I: 63 (100%) | **Location:**  NR  **Histopathology:**  Hst confirmed: 52 (82%)  ACC: 35 (56%)  SCC: 14: 22%)  NOS: 3 (5%)  Undiagnosed: 11 (18%) | **Age:**  78 (56-91)    **Women:**  23 (36%)  **Race:**  NR  **Co-morbidities:**  COPD, advanced age,  other illnesses: 49 (78%)  **Performance status:**  WHO ≤ 2: 63 (100%) |