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 NSCLC2. 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 DLCO10 (3.5-23.3 mL/min/mm Hg)Predicted mean DLCO55% (14-128%)Predicted mean FEV157% (21-111%)**Current or former** **smoker:** 38 (95%)**Performance status:**Median ECOG1 (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: 0Others: 0PBRT 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 NSCLC2. Medically operable**Exclusion criteria:** 1. GOLD COPD class 3-42. FEV1 < 50% of predicted3. DLCO < 50% of predicted4. WHO performance status ≥ 35. 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 COPDNo 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 NSCLC2. 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:**ECOG0: 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

disease1. 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:**WHO0: 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 NSCLC2. 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%) |