## EXCITE Supplementary Online Material, Tables

### Online Material Table 1. EXCITE treatment compliance

| | |
|---|---|
| **Radiotherapy** | |
| Full dose (45 Gy) received without delay as per protocol | 47 (57%) |
| Full dose (45 Gy) received with delay due to adverse events | 29(35%) |
| Dose reduction | 4 (5%) |
| Did not start | 2 (2%) |
| Median dose received in Gy (IQR) | 45 (45-45) |
| | |
| **Irinotecan** | |
| Full dose received (240 mg/m$^2$) without delay | 46 (56%) |
| Full dose received (240 mg/m$^2$) with delay | 10 (12%) |
| Dose reduction | 24 (29%) |
| Did not start | 2 (2%) |
| Number of cycles given | |
| 0 | 2 (2%) |
| 1 | 0 |
| 2 | 5 (6%) |
| 3 | 18 (22%) |
| 4 | 57 (70%) |
| Median dose received (mg/m$^2$) | 238 (180-242) |
| | |
| **Cetuximab** | |
| Full dose received (1650 mg/m$^2$) without delay | 51 (62%) |
| Full dose received (1650 mg/m$^2$) with delay | 9 (11%) |
| Dose reduction | 21 (26%) |
| Did not start | 1 (1%) |
| Number of cycles given | |
| 0 | 1 (1%) |
| 1 | 1 (1%) |
| 2 | 0 (0%) |
| 3 | 2 (2%) |
| 4 | 2 (2%) |
| 5 | 14 (17%) |
| 6 | 62 (76%) |
| Median dose received (mg/m$^2$) | 1650 (1548-1657) |
| | |
| **Capecitabine** | |
| Full dose received without delay | 35 (43%) |
| *Alteration to capecitabine due to: | 45 (55%) |
| treatment not taken | 8 (10%) |
| treatment reduction | 12 (15%) |
| treatment delayed | 4 (5%) |
| treatment not taken and reduced | 9 (11%) |
| treatment not taken and delayed | 1 (1%) |
| treatment reduction and delayed | 9 (11%) |
| treatment not taken, reduced and delayed | 2 (2%) |
| Did not start Capecitabine | 2 (2%) |

*In addition to the central record of the dose of capecitabine prescribed, patients kept a weekly record of prescribed tablets that were not taken

**Online Material Table 2. Details of surgery in the 76 patients undergoing resection[1], together with post operative complications within 30 days of surgery**

| Type of surgery | Number (%) |
|---|---|
| Abdominoperineal excision | 38 (50%) |
| Anterior resection | 36 (47%) |
| Hartmann's procedure | 2 (3%) |
| **Complications within 30 days of surgery** | |
| Anastomotic dehiscence | 3 (4%) |
| Perineal wound dehiscence | 7 (9%) |
| Haemorrhage within the operative field necessitating return to theatre | 1 (1%) |
| Wound infection | 12 (16%) |
| Pelvic infection | 4 (5%) |
| Serious infection elsewhere | 7 (9%) |
| Peritonitis | 2 |
| Pneumonia | 1 |
| Presacral collection | 1 |
| Subphrenic | 1 |
| Cannula site | 1 |
| Urinary sepsis | 1 |
| Re-catheterisation | 12 (16%) |
| Venous thromboembolic event | 1 (1%) |
| Myocardial infarction | 0 (0%) |
| Cerebrovascular accident | 0 (0%) |
| Ventilation required for >24 hours | 0 (0%) |
| Acute respiratory distress syndrome | 0 (0%) |
| Re-admission after discharge | 13 (17%) |
| Death within 30 days of operation | 1 (1%) |
| Other [2] | 9 (12%) |
| Any (of the above) post-surgical complications | 33 (43%) |
| **Time spent on ITU/HDU post-op (days)** | |
| 0 | 32 (42%) |
| 1 | 14 (18%) |
| 2-5 | 15 (20%) |
| 6-10 | 2 (3%) |
| Missing | 13 (17%) |
| Median in days (IQR) | 0.5 (0 to 2) |
| **Total time as in-patient, post-op (days)** | |
| 0 | 1 (1%) |
| 1-10 | 45 (59%) |

| | |
|---|---|
| 11-20 | 14 (18%) |
| 21-30 | 5 (7%) |
| 31-40 | 2 (3%) |
| Missing | 9 (12%) |
| Median in days (IQR) | 8 (5.5 to 12) |

[1]In 4 patients a 'wait and watch' approach was adopted by the treating team because of a complete clinical response to CRT.

[2] Nine patients had 15 grade 3-5 "other" surgical complications post-surgery: One patient had two grade 5 events: ileus and aspiration (and grade 4 vomiting). Two patients had a maximum grade 4 (small bowel obstruction; bleeding associated with surgery). The other six patients had a maximum of grade 3 - abdominal pain (3); DVT (1); type 2 respiratory failure (1); shortness of breath (1); chest infection (1); rectal/pelvic pain (1); oedema (1); low magnesium (1).

**Online Material Table 3. Number of EGFR pathway mutations per sample (including detail of samples containing multiple mutations) in biopsy and resection specimen**

**BIOPSY**

| | Number of samples containing indicated number of EGFR pathway mutations by PS/NGS* | Detail (percentage of mutant DNA) |
|---|---|---|
| No mutation | 28 (36%) | |
| Single mutation | 33 (42%) | - |
| Double mutation | 12 (15%) | KRAS 12 c.35G>A (35%) & KRAS 12 c.35G>T (16.6%)<br>KRAS 12 (33%) & KRAS 13 (5%)<br>KRAS 12 (26%) & KRAS 13 (7%)<br>KRAS 12 (22%) & PIK 545/6 (26%)<br>KRAS 12 (36%) & PIK 542 (27%)<br>KRAS 12 (8%) & BRAF (22%)<br>KRAS 13 (41%) & PIK 545/6 (40%)<br>KRAS 13 (7%) & PIK 542 (9%)<br>KRAS 146 (6%) & NRAS 61 (17%)<br>KRAS 146 (33%) & PIK 545/6 c.(37%)<br>KRAS 146 (5%) & PIK 1047 (7%)<br>BRAF (30%) & PIK 545/6 (25%) |
| Triple mutation | 4 (5%) | KRAS 12 (28%) & KRAS 13 (8%) & PIK 542 (28%)<br>KRAS 12 (9%) & KRAS 13 (5%) & PIK 545/6 (10%)<br>KRAS 146 (9%) & PIK 542 (5%) & PIK 545/6 (5%)<br>KRAS 146 (5%) & PIK 1047 (6%) & PIK 1047 (29%) |
| Quadruple mutation | 1 (1%) | KRAS 12 (5%) & KRAS 12 (6%) & KRAS 12 (5%) & NRAS 12/13 c.35G>A (24%) |
| Total | 78 (100%) | |

**RESECTION**

| | Number of samples containing indicated number of mutations by PS/NGS** | Detail (percentage of mutant DNA) |
|---|---|---|
| No mutation | 20 (37%) | - |
| Single mutation | 26 (48%) | |
| Double mutation | 7 (13%) | KRAS 12 (25%) & KRAS 12 (7%)<br>KRAS 12 c.35G>T (13%) & KRAS 146 c.436G>A (5%)<br>KRAS 12 (18%) & PIK 542 (24%)<br>KRAS 12 (51%) & PIK 542 (5%)<br>KRAS 12 (14%) & PIK 545/6 (10%)<br>KRAS 12 (34%) & PIK 1047 (19%)<br>KRAS 13 (35%) & PIK 542 (26%) |
| Triple mutation | 1 (2%) | KRAS 12 (14%) & KRAS 12 (24%) & KRAS 146 (33%) |
| Total | 54 | |

NA: not applicable; PS: pyrosequencing; NGS: next generation sequencing

*One sample did not have enough DNA to run matched NGS (KRAS 12 mutant on PS)

**Four samples did not have enough DNA to run matched NGS (two non-mutated, one KRAS 12 mutated and one KRAS 13 mutated on PS)