## Supplementary Information

1 of 5

**Pre-EMPT trial Eligibility Criteria**

Eligibility criteria:
Inclusion
1. Participants must be diagnosed with operable oesophageal and gastro-oesophageal adenocarcinoma and scheduled to undergo standard neo-adjuvant chemotherapy and oesophago-gastric surgery as recommended by the Multidisciplinary Meeting decision.
2. 18+
3. </=79 (patients above this age may be included in studies after the feasibility study has been completed)
4. Participants must be able to understand and independently consent to participation in the study.
5. Participants must be able to understand and complete the questionnaires.
6. Participants must be willing to undergo all the standard assessments and interventions included in this study - CPEX testing, blood sampling, questionnaires and exercise intervention where appropriate.
7. Participants must be willing to wear the Fitbit monitoring device and agree with its use.
8. Participants must be ASA 1-3 and fit for surgical resection.
9. Patients should have a Body Mass Index (BMI) equal to or above 18.5 with less than 10% self-reported unintentional weight loss at diagnosis.

Exclusion
Participants will be excluded if they:
1. Are not considered medically fit for surgery at diagnosis, as decided by the Multidisciplinary team
2. Will undergo primary or palliative chemotherapy
3. Are recommended to have chemoradiotherapy
4. Are under 18 years old
5. Are over 79 years old
6. Are unable to undergo CPEX testing
7. Do not wish to take part in selected aspects of the study
8. Cannot or do not wish to attend the CHHP for assessment and/or advice on exercise
9. Cannot understand and give informed consent to the study
10. Cannot understand and complete the questionnaires
11. Do not wish to wear a Fitbit monitoring device
12. ASA 4+
13. Patients with BMI of less than 18.5 with self-reported unintentional weight loss of 10% or more at diagnosis.

## Supplementary Information

### 2 of 5

**Exercise Prehabilitation Program:**
Provided by Centre for Health and Human Performance, London

4 Week, 30 minutes walking programme, with additional Core Strength & Stability, Flexibility and Band Strength Exercises

| | | |
|---|---|---|
| **Week 1** | **SESSION 1** | 30 minutes moderate walk including; 10 x (30s hard walk with 1min 30s easy) |
| | **SESSION 2** | 30 minutes moderate walk including; 2 x (5 x 1 minute hard walk with 1 minute easy) 5 minutes between sets |
| | **SESSION 3** | 30 minutes moderate walk including; 2 x (10 x 30s hard walk with 1min 30s easy) 5 minutes between sets |
| | **SESSION 4** | 30 minutes moderate walk |
| | **SESSION 5** | 30 minutes moderate walk |
| **Week 2** | **SESSION 1** | 30 minutes moderate walk including; 2 x (6 x 1 minute hard walk with 1 minute easy) 5 minutes between sets |
| | **SESSION 2** | 30 minutes moderate walk including; 5 x (2 minutes hard walk with 1 minute easy) 5 minutes between sets |
| | **SESSION 3** | 30 minutes moderate walk including; 10 x (1 minute hard walk with 1 minute easy) 5 minutes between sets |
| | **SESSION 4** | 30 minutes moderate walk |
| | **SESSION 5** | 30 minutes moderate walk |
| **Week 3** | **SESSION 1** | 30 minutes moderate walk including; 2 x (10 x 30s hard walk with 1 minute 30s easy) 15 minutes between sets |
| | **SESSION 2** | 30 minutes moderate walk including; 5 x (3 minutes hard walk with 2 minutes easy) 10 minutes between sets |
| | **SESSION 3** | 30 minutes moderate walk including; 10 x (1 minute hard walk with 1 minute easy) 10 minutes between sets |
| | **SESSION 4** | 30 minutes moderate walk |
| | **SESSION 5** | 30 minutes moderate walk |
| **Week 4** | **SESSION 1** | 30 minutes moderate walk including; 3 x (5 x 30s hard walk with 1 minute 30s easy) 5 minutes between sets |
| | **SESSION 2** | 30 minutes moderate walk including; 10 x (2 minutes hard walk with 1 minute easy) 10 minutes between sets |
| | **SESSION 3** | 30 minutes moderate walk including; 15 x (1 minute hard walk with 1 minute easy) |
| | **SESSION 4** | 30 minutes moderate walk |
| | **SESSION 5** | 30 minutes moderate walk |

***N.B. easy = able to hold full conversation; moderate = brisk walking, concentrating to maintain pace; hard = fast/power walking***

## Supplementary information



*Table 4 Body composition changes*

| Parameters | Intervention Group (n=13) Median (IQR) | Control Group (n=14) Median (IQR) | *p*-value = * |
|---|---|---|---|
| **FFM index (kg/m²)** | | | |
| Baseline | 17.8 (14.4-20.9) | 16.3 (11.8-18.5) | .225 |
| Post-treatment | 18.7 (15.0-20.2) | 14.7 (12.3-17.3) | .026 |
| **FM index (kg/m²)** | | | |
| Baseline | 9.1 (6.4-9.6) | 8.1 (7.1-10.4) | .961 |
| Post-treatment | 8.2 (6.8-9.2) | 8.2 (7.4-10.5) | .698 |
| **FMR** | | | |
| Baseline | 1.08 (0.67-1.75) | 1.07 (0.90-1.58) | .846 |
| Post-treatment | 0.91 (0.59-1.94) | 1.11 (0.88-2.16) | .409 |
| **Visceral fat (cm²)** | | | |
| Baseline | 204 (41-256) | 206 (141-274) | .698 |
| Post-treatment | 154 (104-228) | 214 (163-249) | .207 |
| **Subcutaneous fat (cm²)** | | | |
| Baseline | 153 (109-214) | 165 (112-183) | .808 |
| Post-treatment | 147 (111-227) | 158 (129-190) | .771 |
| **VA/SA ratio** | | | |
| Baseline | 0.83 (0.61-1.51) | 1.24 (0.84-1.50) | .308 |
| Post-treatment | 0.83 (0.59-1.39) | 1.22 (0.99-1.41) | .357 |
| **Weight (kg)** | | | |
| Baseline | 80.1 (64.3-84.3) | 87.5 (68.7-94.5) | .052 |
| Post-treatment | 76.4 (69.2-79.9) | 88.2 (74.0-95.6) | .053 |

** p-values derived from Wilcoxon-signed rank test*

## Supplementary information



*Table 5 Immunity Markers - Baseline versus Post-NAC*

| | **Intervention Group** | | **Control Group** | | |
|---|---|---|---|---|---|
| | **Mean (SD)** | **Range** | **Mean (SD)** | **Range** | ***p*-value =** |
| **CD3** | | | | | |
| Baseline | 1474.38 (649.65) | (683-2793) | 964.94 (350.45) | (582-1587) | |
| Post-NAC | 1681.2 (504.36) | (733-2861) | 981.08 (349.75) | (516-1686) | |
| **Participant change Baseline Post-NAC (%)** | 34.26 (36.58) | (-16.78-111.57) | 4.53 (25.67) | (-23.00-63.41) | **.034** |
| **CD4** | | | | | |
| Baseline | 960.60 (403.63) | (292-2031) | 550.88 (172.49) | (337-971) | |
| Post-NAC | 1117.73 (323.09) | (471-1625) | 584.92 (249.27) | (327-1231) | |
| **Participant change Baseline Post-NAC (%)** | 42.08 (51.40) | (-22.45-179.45) | 9.36 (37.90) | (-26.30-112.17) | .095 |
| **CD8** | | | | | |
| Baseline | 548.50 (394.68) | (174-1678) | 376.75 (227.63) | (134-877) | |
| Post-NAC | 551.47 (297.64) | (182-1267) | 363.33 (179.24) | (120-675) | |
| **Participant change Baseline Post-NAC (%)** | 29.41 (31.19) | (2.82-89.66) | 0.98 (19.69) | (-23.03-50.89) | **.033** |

## Supplementary Information

5 of 5

*Table 6 Inflammatory Markers - Baseline versus Post-NAC*

| | **Intervention Group** | | **Control Group** | | |
|---|---|---|---|---|---|
| | **Mean (SD)** | **Range** | **Mean (SD)** | **Range** | ***p*-value =** |
| **IL-6** | | | | | |
| Baseline | 2.68 (3.76) | (0.16-16.1) | 1.13 (0.65) | (0.41-3.03) | |
| Post-NAC | 3.20 (4.63) | (0.6-19.5) | 2.31 (1.56) | (0.86-6.73) | |
| **Participant change Baseline Post-NAC (%)** | +27.93 (97.02) | (-55.94-275.00) | +126.41 (107.59) | (-53.14-282.39) | .041 |
| **VEGF** | | | | | |
| Baseline | 12.61 (11.98) | (2.66-53.51) | 7.79 (3.43) | (2.92-15.5) | |
| Post-NAC | 9.79 (5.13) | (3.64-21.26) | 9.21 (4.16) | (5.1-17.35) | |
| **Participant change Baseline Post-NAC (%)** | -10.51 (62.09) | (-60.27-149.58) | +51.79 (99.54) | (-67.10-300.34) | .274 |
| **INF-y** | | | | | |
| Baseline | 0.34 (0.38) | (0.1-1.34) | 0.15 (0.17) | (0.01-0.7) | |
| Post-NAC | 0.39 (0.59) | (0.1-2.29) | 0.23 (0.22) | (0.07-0.9) | |
| **Participant change Baseline Post-NAC (%)** | +57.24 (140.13) | (-80.60-300) | +223.64 (562.36) | (-50-1900) | .364 |
| **TNFa** | | | | | |
| Baseline | 1.53 (3.92) | (0.21-16.2) | 0.58 (0.18) | (0.36-0.88) | |
| Post-NAC | 1.76 (4.77) | (0.3-18.99) | 0.74 (0.31) | (0.41-1.5) | |
| **Participant change Baseline Post-NAC (%)** | -1.77 (33.23) | (-53.03-45.45) | +28.31 (74.51) | (-30.99-233.33) | .245 |
| **MCP-1** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Baseline | 54.14 (32.62) | (12.73-136.33) | 39.98 (27.82) | (4.24-95.7) | |
| Post-NAC | 60.94 (21.18) | (16.8-97.63) | 63.37 (33.18) | (24.68-137.2) | |
| **Participant change Baseline Post-NAC (%)** | +52.11 (58.18) | (-34.01-174.16) | +163.69 (193.53) | (-45.56-482.08) | .093 |
| **EGF** | | | | | |
| Baseline | 2.71 (3.13) | (0.34-12.4) | 6.96 (7.32) | (0.5-24.5) | |
| Post-NAC | 3.38 (6.25) | (0.4-25.2) | 2.87 (3.30) | (0.6-12.5) | |
| **Participant change Baseline Post-NAC (%)** | +20.06 (80.48) | (-62.72-176.47) | -8.23 (152.86) | (-95.21-440.00) | .607 |