# Supplementary materials: Phase 1 Study to Evaluate the Safety of Reducing the Prophylactic Dose of Dexamethasone around Docetaxel Infusion in Patients with Prostate and Breast Cancer

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**Table S1.** Differences between dose levels for Glucose, Insulin and IGF-1 levels in patient with prostate cancer.

| Dose level | 1 (n=5) | 2 (n=6) | 3A (n=6) | 3B (n=5) | p-value** |
|---|---|---|---|---|---|
| Glucose mmol/L* | 6.92 (2.77) | 6.57 (0.76) | 7.01 (1.99) | 5.87 (1.84) | 0.77 |
| Insulin mIU/L* | 36.60 (39.39) | 32.23 (23.64) | 47.42 (72.56) | 27.13 (33.23) | 0.67 |
| IGF-1 nmol/L* | 16.10 (6.94) | 16.36 (8.89) | 16.86 (46.54) | 18.03 (11.47) | 0.92 |

* Median (IQR), **Kruskal Wallis test; Abbreviations: IGF-1: Insulin-like growth factor.

**Table S2.** Quality of Life scores for evaluable patients at baseline (Mean, SD).

| **Prostate cancer** | **Cohort 1 (n=6)** | **Cohort 2 (n=6)** | **Cohort 3 (n=12)** | ***p* value** |
|---|---|---|---|---|
| EORTC QoL-C30 domains | | | | |
| Global Health | 65.3 (33.9) | 50.0 (26.4) | 81.3 (17.9) | 0.15 |
| Physical functioning | 73.3 (29.5) | 80.0 (14.6) | 92.8 (12.2) | 0.20 |
| Role functioning | 63.9 (40.0) | 72.2 (34.4) | 88.9 (20.5) | 0.34 |
| Emotional functioning | 80.6 (12.5) | 84.7 (17.8) | 84.0 (14.4) | 0.44 |
| Cognitive functioning | 72.2 (37.5) | 80.6 (16.4) | 88.9 (16.4) | 0.38 |
| Social functioning | 66.7 (42.2) | 83.3 (21.1) | 90.3 (20.7) | 0.54 |
| EORTC QoL-C30 symptoms | | | | |
| Fatigue | 38.9 (37.0) | 27.8 (26.1) | 13.0 (17.6) | 0.62 |
| Nausea | 5.6 (8.6) | 0.0 (0.0) | 0.0 (0.0) | **0.04** |
| Pain | 25.0 (39.1) | 25.0 (25.3) | 5.6 (19.2) | 0.08 |
| Dyspnea | 11.1 (17.2) | 27.8 (25.1) | 13.9 (30.0) | 0.35 |
| Insomnia | 33.3 (42.2) | 22.2 (27.2) | 16.7 (30.2) | 0.73 |
| Appetite loss | 22.2 (40.4) | 0.0 (0.0) | 5.6 (13.0) | 0.36 |
| Constipation | 5.6 (13.6) | 11.1 (17.2) | 2.8 (9.6) | 0.41 |
| Diarrhea | 16.7 (40.8) | 5.6 (13.6) | 8.3 (15.1) | 0.34 |
| Financial difficulties | 22.2 (40.4) | 5.6 (13.6) | 5.6 (13.0) | 0.53 |
| **Breast cancer** | **Cohort 1 (n=3)** | **Cohort 2 (n=6)** | **Cohort 3 (n=1)** | ***p* value** |
| EORTC QoL-C30 domains | | | | |
| Global Health | 66.7 (16.7) | 73.6 (26.0) | 66.7 | 0.35 |
| Physical functioning | 77.8 (20.4) | 86.7 (8.2) | 80.0 | 0.40 |
| Role functioning | 55.6 (9.6) | 58.3 (32.9) | 33.3 | 0.12 |
| Emotional functioning | 91.7 (8.3) | 77.8 (21.5) | 66.7 | 0.08 |

| | | | | |
|---|---|---|---|---|
| Cognitive functioning | 77.8 (9.6) | 75.0 (17.5) | 66.7 | 0.77 |
| Social functioning | 88.9 (19.2) | 69.4 (38.6) | 66.7 | 0.40 |
| EORTC QoL-C30 symptoms | | | | |
| Fatigue | 37.0 (17.0) | 50.0 (33.5) | 55.6 | 0.82 |
| Nausea | 11.1 (9.6) | 20.0 (21.7) | 0.0 | 0.68 |
| Pain | 27.8 (9.6) | 25.0 (37.6) | 0.0 | 0.21 |
| Dyspnea | 11.1 (19.2) | 38.9 (25.1) | 33.3 | 0.41 |
| Insomnia | 55.6 (19.2) | 33.3 (36.5) | 33.3 | 0.29 |
| Appetite loss | 0.0 (0.0) | 33.3 (21.1) | 66.7 | **0.03** |
| Constipation | 55.6 (50.9) | 22.2 (27.2) | 0.0 | 0.57 |
| Diarrhea | 11.1 (19.2) | 11.1 (17.2) | 33.3 | 0.44 |
| Financial difficulties | 22.2 (19.2) | 5.6 (13.6) | 0.0 | 0.24 |

Abbreviations: EORTC: European Organization for Research and Treatment of Cancer-Core, QoL: Quality of Life.

**Table S3.** Changes in scores from baseline for patients with prostate cancer.

| | | **Questionnaire time points** | | | **p-value** | | |
|---|---|---|---|---|---|---|---|
| | | **Baseline** | **After 3 cycles** | **After 6 cycles** | **Time** | **Cohort** | **Time by Cohort** |
| Global Health | Cohort 1 | 68.3 | 86.1 | 70.0 | 0.84 | 0.05 | 0.63 |
| | Cohort 2 | 36.11 | 45.8 | 54.2 | | | |
| | Cohort 3 | 78.3 | 77.1 | 72.9 | | | |
| **Functioning scales** | | | | | | | |
| Physical functioning | Cohort 1 | 77.3 | 93.3 | 81.3 | **0.03** | 0.11 | **0.03** |
| | Cohort 2 | 71.1 | 56.7 | 60.0 | | | |
| | Cohort 3 | 91.3 | 90.8 | 74.1 | | | |
| Role functioning | Cohort 1 | 70.0 | 77.8 | 66.7 | 0.06 | 0.12 | 0.06 |
| | Cohort 2 | 44.4 | 16.7 | 33.3 | | | |
| | Cohort 3 | 86.7 | 79.2 | 60.4 | | | |
| Emotional functioning | Cohort 1 | 83.3 | 83.3 | 81.7 | 0.77 | 0.31 | 0.81 |
| | Cohort 2 | 72.2 | 70.8 | 58.3 | | | |
| | Cohort 3 | 83.3 | 85.4 | 82.3 | | | |
| Cognitive Functioning | Cohort 1 | 66.7 | 88.9 | 73.3 | 0.44 | 0.34 | 0.44 |
| | Cohort 2 | 72.2 | 75.0 | 91.7 | | | |
| | Cohort 3 | 86.7 | 91.7 | 83.3 | | | |
| Social functioning | Cohort 1 | 73.3 | 88.9 | 73.3 | 0.49 | 0.34 | 0.59 |
| | Cohort 2 | 77.8 | 50.0 | 58.3 | | | |
| | Cohort 3 | 91.7 | 89.6 | 83.3 | | | |
| **Symptoms** | | | | | | | |
| Fatigue | Cohort 1 | 35.6 | 40.7 | 48.9 | **0.02** | 0.13 | 0.06 |
| | Cohort 2 | 48.1 | 61.1 | 66.7 | | | |
| | Cohort 3 | 14.4 | 23.8 | 37.5 | | | |
| Nausea | Cohort 1 | 6.7 | 0.0 | 6.7 | **0.03** | 0.20 | **0.04** |
| | Cohort 2 | 0.0 | 0.0 | 16.7 | | | |
| | Cohort 3 | 0.0 | 0.0 | 6.3 | | | |
| Pain | Cohort 1 | 30.0 | 5.6 | 3.3 | 0.53 | 0.23 | 0.06 |
| | Cohort 2 | 38.9 | 33.3 | 50.0 | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Cohort 3 | 6.7 | 12.5 | 35.4 | | | |
| Dyspnea | Cohort 1 | 13.3 | 0.0 | 33.3 | **<0.01** | 0.39 | **0.02** |
| | Cohort 2 | 33.3 | 16.7 | 50.0 | | | |
| | Cohort 3 | 13.3 | 8.3 | 33.3 | | | |
| Insomnia | Cohort 1 | 26.7 | 33.3 | 33.3 | 0.18 | 0.60 | 0.40 |
| | Cohort 2 | 33.3 | 16.7 | 66.7 | | | |
| | Cohort 3 | 20.0 | 8.3 | 33.3 | | | |
| Appetite loss | Cohort 1 | 26.7 | 0.0 | 20.0 | 0.69 | 0.16 | **0.04** |
| | Cohort 2 | 0.0 | 0.0 | 50.0 | | | |
| | Cohort 3 | 6.7 | 0.0 | 12.5 | | | |
| Constipation | Cohort 1 | 6.7 | 0.0 | 6.7 | 0.56 | 0.17 | 0.93 |
| | Cohort 2 | 22.2 | 0.0 | 16.7 | | | |
| | Cohort 3 | 3.33 | 4.2 | 4.2 | | | |
| Diarrhea | Cohort 1 | 20.0 | 11.1 | 20.0 | 0.76 | 0.45 | 0.98 |
| | Cohort 2 | 0.0 | 0.0 | 0.0 | | | |
| | Cohort 3 | 10.0 | 4.2 | 12.5 | | | |
| Financial difficulties | Cohort 1 | 26.7 | 0.0 | 13.3 | 0.08 | 0.10 | **0.02** |
| | Cohort 2 | 11.1 | 0.0 | 0.0 | | | |
| | Cohort 3 | 3.33 | 4.2 | 0.0 | | | |

P Time: changes of QoL scores over time; P Cohort: differences in QoL scores between cohorts; P Time by Cohort: different effects between cohorts over time.

**Table S4.** (A)Occurrence of hypersensitivity reactions (HSR) and fluid retention in evaluable patients with breast cancer; (B) Occurrence of hypersensitivity reactions (HSR) and fluid retention in evaluable patients with prostate cancer.

*(A) Occurrence of hypersensitivity reactions (HSR) and fluid retention in evaluable patients with breast cancer*

| *Patient* | *Cohort* | *TNM classification* | *Receptor status* | *Treatment* | *Docetaxel treatment* | *Cycles of Docetaxel* | *Cumulative dose of Docetaxel* | *HSR (any grade)* | *HSR (grade III/IV)* | *Fluid retention (any grade)* | *Fluid retention (grade III/IV)* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***1102*** | 1 | T2N0M0 | TNBC | Neo-adjuvant | Monotherapy 100 mg/m² | 4 | 375 mg/m² | - | - | - | - |
| ***1104*** | 1 | T1N0M0 | ER+, PR/Her2- | Adjuvant | Monotherapy 100 mg/m² | 4 | 400 mg/m² | - | - | - | - |
| ***1105*** | 1 | T2N1M0 | ER/PR+, Her2- | Adjuvant | Monotherapy 100 mg/m² | 4 | 340 mg/m² | - | - | - | - |
| ***1106*** | 1 | T2N1M0 | ER/PR+, Her2- | Neo-adjuvant | Monotherapy 100 mg/m² | 4 | 340 mg/m² | - | - | - | - |
| ***1107*** | 1 | T1N0M0 | ER/PR+, Her2- | Adjuvant | Monotherapy 100 mg/m² | 4 | 325 mg/m² | - | - | - | - |
| ***1108*** | 1 | T1N1M0 | ER/PR+, Her2- | Adjuvant | Monotherapy 100 mg/m² | 4 | 325 mg/m² | - | - | Grade 1 edema | - |
| ***1201*** | 2 | T2N1M0 | ER/PR+, Her2- | Neo-adjuvant | Monotherapy 100 mg/m² | 4 | 340 mg/m² | - | - | Grade 2 edema | - |
| ***1202*** | 2 | T3N3M0 | TNBC | Neo-adjuvant | Monotherapy 100 mg/m² | 4 | 307 mg/m² | - | - | - | - |
| ***1203*** | 2 | T2N0M0 | TNBC | Neo-adjuvant | Monotherapy 100 mg/m² | 4 | 400 mg/m² | - | - | - | - |
| ***1204*** | 2 | T1N0M) | ER/PR+, Her2- | Adjuvant | Combination therapy* 75 mg/m² | 4 | 300 mg/m² | - | - | - | - |
| ***1205*** | 2 | T2N1M0 | ER+, PR/Her2- | Neo-adjuvant | Monotherapy 100 mg/m² | 1 | 100 mg/m² | - | - | - | - |
| ***1206*** | 2 | T2N0M0 | TNBC | Neo-adjuvant | Monotherapy 100 mg/m² | 4 | 400 mg/m² | - | - | - | - |
| ***1303*** | 3 | T1N1M0 | ER+, PR/Her2- | Neo-adjuvant | Monotherapy 100 mg/m² | 6 | 600 mg/m² | - | - | - | - |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***1304*** | 3 | T2N1M1 | ER/PR+, Her2+ | Palliative | Combination therapy** 100 mg/m² | 6 | 450 mg/m² | - | - | - | - |

***(B) Occurrence of hypersensitivity reactions (HSR) and fluid retention in evaluable patients with prostate cancer***

| *Patient* | *Cohort* | *Disease* | *Treatment* | *Docetaxel treatment* | *Cycles of Docetaxel* | *Cumulative dose of Docetaxel* | *HSR (any grade)* | *HSR (grade III/IV)* | *Fluid retention (any grade)* | *Fluid retention (grade III/IV)* |
|---|---|---|---|---|---|---|---|---|---|---|
| ***2101*** | 1 | mCRPC | Palliative | Monotherapy 75 mg/m² | 1 | 75 mg/m² | - | - | - | - |
| ***2102*** | 1 | mCRPC | Palliative | Monotherapy 75 mg/m² | 9 | 645 mg/m² | - | - | - | - |
| ***2103*** | 1 | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2104*** | 1 | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2105*** | 1 | mCRPC | Palliative | Monotherapy 75 mg/m² | 8 | 600 mg/m² | - | - | - | - |
| ***2106*** | 1 | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | - | - | Grade 2 edema | - |
| ***2201*** | 2 | mCRPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2202*** | 2 | mCRPC | Palliative | Monotherapy 75 mg/m² | 5 | 375 mg/m² | - | - | - | - |
| ***2203*** | 2 | mCRPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2204*** | 2 | mCRPC | Palliative | Monotherapy 75 mg/m² | 3 | 225 mg/m² | - | - | - | - |
| ***2205*** | 2 | mCRPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2206*** | 2 | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | Grade 1** | - | - | |
| ***2207*** | 2 | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | | | | |
| ***2301*** | 3A | mCRPC | Palliative | Monotherapy 75 mg/m² | 5 | 281 mg/m² | | | | |
| ***2302*** | 3A | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | | | | |
| ***2303*** | 3A | mHSPC | Palliative | Monotherapy 75 mg/m² | 6 | 450 mg/m² | | | | |
| ***2304*** | 3A | mHSPC | Palliative | Monother- | 6 | 450 mg/m² | - | - | Grade 1 | - |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | apy 75 mg/m² | | | | | edema | |
| ***2305*** | 3A | mHSPC | Palliative | Monother-apy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2306*** | 3A | mCRPC | Palliative | Monother-apy 75 mg/m² | 2 | 150 mg/m² | - | | | |
| ***2401*** | 3B | mHSPC | Palliative | Monother-apy 75 mg/m² | 6 | 450 mg/m² | | | | |
| ***2402*** | 3B | mHSPC | Palliative | Monother-apy 75 mg/m² | 5 | 356 mg/m² | | | | |
| ***2403*** | 3B | mHSPC | Palliative | Monother-apy 75 mg/m² | 6 | 450 mg/m² | - | - | Grade 1 edema | - |
| ***2405*** | 3B | mHSPC | Palliative | Monother-apy 75 mg/m² | 6 | 450 mg/m² | - | - | Grade 2 edema | - |
| ***2407*** | 3B | mHSPC | Palliative | Monother-apy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |
| ***2409*** | 3B | mHSPC | Palliative | Monother-apy 75 mg/m² | 6 | 450 mg/m² | - | - | - | - |

(A)* Docetaxel – cyclophosphamide ** Docetaxel – trastuzumab – pertuzumab; Abbreviations: TNBC: triple negative breast cancer; ER: Estrogen receptor; PR: progesterone receptor; Her2: human epidermal growth factor receptor 2; (B)** After a grade 1 HSR at the first cycle of docetaxel this patient decided to use the normal dosage of dexamethasone in the consequent cycles and he went off study; Abbreviations: mHSPC: metastatic Hormone-sensitive prostate cancer; mCRPC: metastatic castration-resistant prostate cancer.