**SUPPLEMENTAL MATERIAL**

Supplemental Table 1. Comparison of inclusion and exclusion criteria with the CHAARTED trial.

|  |  |  |
| --- | --- | --- |
| **CHAARTED trial criteria** | **Corresponding criterion in real-world****(yes/no)** | **Description of corresponding real-world criterion/justification for lack of corresponding criterion** |
| ***Inclusion criteria*** |
| Patients must have histologically or cytologically confirmed prostate cancer | yes | At least one inpatient or confirmed outpatient diagnoses of prostate cancer (see Supplemental Table 2 for diagnostic codes) in the inclusion period (01/01/2014-31/12/2019). |
| Metastatic disease | yes | At least one inpatient or outpatient diagnosis of a metastasis within 365 days from a PC diagnosis in the inclusion period (see Supplemental Table 2 for diagnostic codes). |
| Experimental arm: Androgen-Deprivation Therapy and Docetaxel.Active comparator: Androgen-Deprivation Therapy alone. | yes | At least one outpatient prescription or inpatient administration of docetaxel or ADT after first diagnosis of a metastasis in the inclusion period (see Supplemental Table 2 for ATC and OPS codes).Index date = earliest date of ADT or docetaxel prescription.  |
| At least 18 years of age | yes | Age 18 or older at index |
| On androgen-deprivation therapy for < 120 days.Prior hormonal therapy allowed provided the following are true:* Therapy was discontinued ≥ 12 months ago AND there is no evidence of disease, as defined by 1 of the following:
* PSA < 0.1 ng/dL after prostatectomy plus hormonal therapy
* PSA < 0.5 ng/dL and has not doubled above nadir after radiotherapy plus hormonal therapy
* Therapy lasted no more than 24 months
* Last depot injection must have expired by the 24-month mark
 | yes | No ADT prescriptions before 120 days prior to index.ADT allowed more than 120 days prior to index if:* Last ADT prescription day supply exhausted at least 12 months prior to index
* First ADT prescription no more than 24 months before exhaustion of supply of last ADT prescription

No data on PSA available. |
| At least 4 weeks since prior major surgery and recovered from all toxicity prior to randomization | yes | No evidence of inpatient surgery (see Supplemental Table 2 for OPS codes) within a hospitalization with at least one overnight stay in the 28 days prior to index |
| Prior palliative radiotherapy allowed if commenced within 30 days before starting androgen deprivation | yes | No evidence of radiotherapy (see Supplemental Table 2 for OPS and EBM codes) before 30 days prior to index |
| Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-2 | no | No ECOG score available in data |
| Organ function that was adequate for docetaxel treatment* Absolute neutrophil count ≥ 1,500/mm^3
* Platelet count ≥ 100,000/mm^3
* Bilirubin ≤ upper limit of normal (ULN)
* Alanine aminotransferase (ALT) ≤ 2.5 times ULN
* Creatinine clearance ≥ 30 mL/min
* Prothrombin time (PT) and international normalized ratio (INR) ≤ 1.5 times ULN (unless on therapeutic anticoagulation)
* Partial thromboplastin time (PTT) ≤ 1.5 times ULN (unless on therapeutic anticoagulation)
 | no | No laboratory test results available in data |
| ***Exclusion criteria*** |
| Prior malignancy in the past 5 years except for basal cell or squamous cell carcinoma of the skin | yes | At least one inpatient or outpatient diagnosis of a primary cancer other than PC, basal cell or squamous cell carcinoma of the skin in the baseline period (see Supplemental Table 2 for diagnostic codes) |
| Active cardiac disease, including the following:* Active angina
* Symptomatic congestive heart failure
* Myocardial infarction within the past 6 months
 | yes | At least one inpatient diagnosis of active angina, congestive heart failure, or myocardial infarction (see Supplemental Table 2 for diagnostic codes) in the 6 months prior to index  |
| Prior chemotherapy in adjuvant or neoadjuvant setting | yes | At least one outpatient prescription or inpatient administration of docetaxel, cabazitaxel, mitoxantrone, or estramustine, during baseline (see Supplemental Table 2 for codes) |
| Prostate-specific antigen (PSA) level has risen and met criteria for progression from its lowest point between the start of androgen-deprivation therapy and randomization | no | PSA level not provided in data |
| Peripheral neuropathy > grade 1 | no | Peripheral neuropathy grade not available in the data |
| History of severe hypersensitivity reaction to docetaxel or other drugs formulated with polysorbate 80 | no | Not available in the data |

Supplemental Table 2. Codes for identification of diagnoses, drug prescriptions/administrations, and procedures in German claims data.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Diagnosis/drug/procedure** | **ICD-10-GM** | **ATC** | **OPS** | **EBM** |
| Prostate cancer | C61% | - | - | - |
| Metastatic cancer | C77%, C78%, C79%, C80% | - | - | - |
| Docetaxel | - | L01CD02 | 6-002.h | - |
| ADT (LHRH agonist or antagonist, surgical castration) | - | **LHRH agonists:** H01CA04, L02AE02, H01CA05, L02AE03, H01CA07, L02AE05**LHRH antagonists:** L02BX02 | - | **Orchiectomy**: 5-622% |
| Surgical procedure in the inpatient setting within a hospitalization with at least one overnight stay | - | - | - | 5% |
| Radiotherapy | Z51.0 | - | 8-520 to 8-529, 8-52a, 8-52b, 8-52c, 8-530, 8-531, 8-539 | 25210, 25211, 25213, 25214, 25228-25230, 25310, 25320-25323, 25330-25333, 25340-25342, 32012, 40500, 40502, 40504, 40506, 40508, 40510, 40512, 40514, 40516, 40518, 40520, 40522, 40524, 40526, 20528, 40530, 40532, 40534, 40536, 40538, 40540, 40546, 40548, 40550-40552, 40554, 40556, 40558, 40560, 40562, 40568, 40576, 40580, 40582, 40584, 40840, 40841, 17210, 17214, 17228, 17310, 17311, 17320, 17321, 17330, 17331, 17332, 17333, 17340, 17341, 17350, 17351, 17360-17363, 17370-17373 |
| Primary cancer other than PC, basal cell or squamous cell carcinoma of the skin | C00%-C75% except C61% and C44%; C81%-C96 | - | - | - |
| Angina | I20% | - | - | - |
| Congestive heart failure  | I11%, I50% | - | - | - |
| Myocardial infarction | I21%, I22% | - | - | - |
| Chemotherapy agents | - | **Docetaxel**: L01CD02 **cabazitaxel:** L01CD04 **mitoxantrone:** L01DB07 **estramustine:** L01XX11 | **Docetaxel**: 6-002.h **cabazitaxel:** 6-006.1 | - |
| Abiraterone | - | L02BX03 | 6-006.2 | - |
| Enzalutamide | - | L02BB04 | 6-007.6 | - |
| Liver disease | B18%, K70%, K73%, K75%, K72%, K74%, I85% | - | - | - |
| Biliary disease | K80%, K81%, K82%, K83% | - | - | - |
| Renal disease  | N17%, N18%, N19% | - | - | - |
| Cardiac disease | I20%, I21%, I252%, I11%, I50% | - | - | - |
| Pleural effusion  | J90%, J91% | - | - | - |

**Supplemental Table 3. Baseline characteristics in unmatched and matched cohorts, 1:2 matching.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Mean** | **Bias** |  |
|  | *Treated* | *Control*  | *%bias* | *% reduction bias* | *p-value* |
| **Age** |  |  |  |  |  |
|  Unmatched | 67.507 | 74.448 | -96.2 |  | **0.000** |
|  Matched | 66.703 | 66.081 | 7.5 | 92.2 | 0.594 |
| **CCI** |  |  |  |  |  |
|  Unmatched | 9.56 | 10.055 | -26.1 |  | 0.053 |
|  Matched | 9.5811 | 9.1554 | 22.5 | 13.9 | 0.137 |
| **Number inpatient visits** |  |  |  |  |  |
|  Unmatched | 1.92 | 1.5902 | 21.7 |  | 0.077 |
|  Matched | 1.8784 | 1.6824 | 12.9 | 40.6 | 0.437 |
| **Number outpatient visits** |  |  |  |  |  |
|  Unmatched | 6.8 | 7.3689 | -26.3 |  | **0.038** |
|  Matched | 6.8243 | 6.2162 | 28.1 | -6.9 | 0.138 |
| **Biliary disease** |  |  |  |  |  |
|  Unmatched | .06667 | .06557 | 0.4 |  | 0.972 |
|  Matched | .06757 | .06801 | 2.7 | -518.2 | 0.868 |
| **Liver disease** |  |  |  |  |  |
|  Unmatched | .05333 | .04372 | 4.5 |  | 0.716 |
|  Matched | .05405 | .04054 | 6.3 | -40.5 | 0.701 |
| **Pleural effusion** |  |  |  |  |  |
|  Unmatched | .01333 | .03005 | -11.5 |  | 0.419 |
|  Matched | .01351 | .02027 | -4.6 | 59.6 | 0.752 |
| **Renal disease** |  |  |  |  |  |
|  Unmatched | .25333 | .28142 | -6.3 |  | 0.621 |
|  Matched | .25676 | .16216 | 21.3 | -236.8 | 0.159 |
| **Cardiac disease** |  |  |  |  |  |
|  Unmatched | .08 | .10109 | -7.3 |  | 0.576 |
|  Matched | .08108 | .04054 | 14.1 | -92.2 | 0.305 |
| **Hospitalization days** |  |  |  |  |  |
|  Unmatched | 14.547 | 11.74 | 13.5 |  | 0.211 |
|  Matched | 14.703 | 15.277 | -2.8 | 79.5 | 0.889 |

Boldface denotes statistical significance at the 95% confidence level.

**Supplemental Table 4. Overall survival in the CHAARTED trial and in German claims data, matched cohorts 1:2 matching.**

|  |  |  |
| --- | --- | --- |
| **Group** | **CHAARTED Trial** | **German claims data (matched cohorts)** |
|   | Median Age | Median Survival | Median Follow Up  | Hazard Ratio | Median Age | Median Survival | Median Follow Up  | Hazard Ratio |
| (95% CI) | (95% CI) |
| ADT | 63 years | 47.2 months | 53.7 months | 0.72 | 65 years | 37.9 months | 22.8 months | 0.75 |
| Docetaxel  | 64 years | 57.6 months | (0.59-0.89) | 67 years | not reached | (0.44-1.25) |

Proportional hazard test (Schoenefeld residuals): p=0.763

**Supplemental Table 5. Baseline characteristics of weighted cohorts.**

|  |  |  |
| --- | --- | --- |
|  | **Mean** |  |
|  | *Treated* | *Control*  | *p-value* |
| **Age** | 70.2 | 73.0 | **0.011** |
| **CCI** | 9.5 | 10.0 | 0.055 |
| **Number inpatient visits** | 1.6 | 1.7 | 0.871 |
| **Number outpatient visits** | 7.1 | 7.3 | 0.475 |
| **Biliary disease** | 0.0 | 0.1 | 0.583 |
| **Liver disease** | 0.0 | 0.0 | 0.955 |
| **Pleural effusion** | 0.0 | 0.0 | 0.741 |
| **Renal disease** | 0.2 | 0.3 | 0.292 |
| **Cardiac disease** | 0.1 | 0.1 | 0.323 |
| **Hospitalization days** | 11.6 | 12.2 | 0.767 |

**Supplemental Table 6. Overall survival in the CHAARTED trial and in German claims data, weighted cohorts.**

|  |  |  |
| --- | --- | --- |
| **Group** | **CHAARTED Trial** | **German claims data (weighted cohorts)** |
|   | Median Age | Median Survival | Median Follow Up  | Hazard Ratio | Median Age | Median Survival | Median Follow Up  | Hazard Ratio |
| (95% CI) | (95% CI) |
| ADT | 63 years | 47.2 months | 53.7 months | 0.72 | 74 years | 37 months | 22.3 months | 0.86 |
| Docetaxel  | 64 years | 57.6 months | (0.59-0.89) | 70 years | 37.3 months | 0.52-1.43 |

Proportional hazard test (Schoenefeld residuals): p=0.368