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Adding abiraterone or docetaxel to long-term hormone therapy for prostate cancer: directly randomised data from the STAMPEDE multi-arm, multi-stage platform protocol


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Note: This study was previously presented at the European Society of Medical Oncology Conference in Madrid, Spain (8 September 2017).

Background: Adding abiraterone acetate with prednisolone (AAP) or docetaxel with prednisolone (DocP) to standard-of-care (SOC) each improved survival in systemic therapy for advanced or metastatic prostate cancer: evaluation of drug efficacy: a multi-arm multi-stage platform protocol recruiting patients with high-risk locally advanced or metastatic PCa starting long-term androgen deprivation therapy (ADT). The protocol provides the only direct, randomised comparative data of SOC + AAP versus SOC + DocP.

Method: Recruitment to SOC + DocP and SOC + AAP overlapped November 2011 to March 2013. SOC was long-term ADT or, for most non-metastatic cases, ADT for ≥2 years and RT to the primary tumour. Stratified randomisation allocated pts 2 : 1 : 2 to SOC + docetaxel 75 mg/m² 3-weekly × 6 + prednisolone 10 mg daily; or SOC + abiraterone acetate 1000 mg + prednisolone 5 mg daily. AAP duration depended on stage and intent to give radical RT. The primary outcome...
measure was death from any cause. Analyses used Cox proportional hazards and flexible parametric models, adjusted for stratification factors. This was not a formally powered comparison. A hazard ratio (HR) < 1 favours SOC + AAP, and HR > 1 favours SOC + DocP.

**Results:** A total of 566 consenting patients were contemporaneously randomised: 189 SOC + DocP and 377 SOC + AAP. The patients, balanced by allocation treatment were: 342 (60%) M1; 429 (76%) Gleason 8–10; 449 (79%) WHO performance status 0; median age 66 years and median PSA 56 ng/ml. With median follow-up 4 years, 149 deaths were reported. For overall survival, HR = 1.16 (95% CI 0.82–1.65); failure-free survival HR = 0.51 (95% CI 0.39–0.67); progression-free survival HR = 0.65 (95% CI 0.48–0.88); metastasis-free survival HR = 0.77 (95% CI 0.57–1.03); prostate cancer-specific survival HR = 1.02 (0.70–1.49); and symptomatic skeletal events HR = 0.83 (95% CI 0.55–1.25). In the safety population, the proportion reporting ≥ 1 grade 3, 4 or 5 adverse events ever was 36%, 13% and 1% SOC + DocP, and 40%, 7% and 1% SOC + AAP; prevalence 11% at 1 and 2 years on both arms. Relapse treatment patterns varied by arm.

**Conclusions:** This direct, randomised comparative analysis of two new treatment standards for hormone-naive prostate cancer showed no evidence of a difference in overall or prostate cancer-specific survival, nor in other important outcomes such as symptomatic skeletal events. Worst toxicity grade over entire time on trial was similar but comprised different toxicities in line with the known properties of the drugs.

**Trial registration:** Clinicaltrials.gov: NCT00268476.

**Key words:** prostate cancer, randomised, treatment, abiraterone, docetaxel, head-to-head

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**Research in context**

**Evidence before this study**

Abiraterone acetate plus prednisone/prednisolone (AAP) and docetaxel with prednisone/prednisolone (DocP) have separately been shown to improve survival when used in addition to the previous international standard-of-care (SOC) for hormone-sensitive prostate cancer of androgen deprivation therapy with further therapy such as AAP or DocP on relapse. This has been confirmed in a number of separate trials and on meta-analysis. The largest body of evidence for both AAP and DocP comes from the systemic therapy for advanced or metastatic prostate cancer: evaluation of drug efficacy (STAMPEDE) platform trial.

**Added value of this study**

Recruitment to DocP and AAP overlapped in STAMPEDE giving the only head-to-head evidence comparing these two new standard treatment approaches. We report data from the 566 patients who were directly randomised between these two treatment approaches while the two research arms were both open to recruitment. The data show strong evidence favouring SOC + AAP on earlier, more biochemically driven outcome measures (OMs). For longer-term, more clinically driven OMs, including bone complications, prostate cancer-specific and overall survival, there is no evidence of a significant difference between AAP and DocP.

**Implications of all the available evidence**

The reported trials and meta-analyses showed a larger effect on survival for AAP over the previous SOC than did DocP over the standard SOC. These data show that the story may be more complicated. No other directly randomised data on survival of these treatments are available. Individual patient data network meta-analysis using all of the published trials are warranted, accounting for differences in patient characteristics, treating clinicians and centres and salvage treatment access. The STAMPEDE team is collaborating with the STOPCAP meta-analysis group to achieve this.
Methods

Trial design

The STAMPEDE protocol and design have been described in detail elsewhere [7, 10, 12, 14]. Briefly, STAMPEDE comprises a series of multi-arm multi-stage (MAMS) comparisons that have overlapped in recruitment and follow-up time.

Patient selection

Eligible patients were those starting long-term ADT for the first time. This was defined as patients with metastatic disease, nodal involvement or node negative, non-metastatic disease with two or more of three high-risk features: T-category 3 or 4, Gleason sum score 8–10 or PSA > 40 ng/ml. Patients rapidly relapsing after previous local therapy were also permitted if they had PSA > 20 ng/ml or PSA > 4 ng/ml with a PSA doubling time <6 months or those who developed loco-regional or metastatic spread whilst not on hormone therapy.

As with all STAMPEDE comparisons, the primary OM of the two underpinning comparisons (against control) was OS. Failure-free survival (FFS) was an intermediate primary OM, defined as time from randomisation to the first of: rising PSA (where rising PSA was defined as a confirmed rise to >4 ng/ml, and >50% above the lowest value in the first 6 months after randomisation); new disease or progression of: distant metastases, lymph nodes or local disease; or death from prostate cancer. Progression-free survival (PFS) was defined as time from randomisation to the first of: new disease or progression of: distant metastases, lymph nodes or local disease; or death from prostate cancer [15]. Metastatic PFS (MPFS) was defined as time from randomisation to death from any cause, new metastases or progression of distant metastases.

All patients provided written informed consent; all versions of the protocol have been reviewed by the relevant research ethics committees and the regulatory agencies; the original protocol and all subsequent versions involving the introduction of a new research arm and comparison were independently peer-reviewed by Cancer Research UK (CRUK).

Patients have been allocated across a number of research treatments as depicted in Figure 1. Here we focus on those patients randomised between 15 November 2011 and 31 March 2013, while both the ‘docetaxel comparison’ and the ‘abiraterone comparison’ were open to recruitment, and who were allocated to either SOC + DocP or SOC + AAP.

Trial treatment, masking and follow-up

The SOC was long-term hormone therapy with LHRH analogues (with short term antiandrogen if relevant) or orchidectomy. Unless contraindicated, radiotherapy to the prostate was mandated in all patients with N0M0 disease, encouraged in patient with N + M0 disease, and permitted in patients with M1 disease until the activation of the ‘M1 | RT comparison’ in January 2013. On the DocP arm, docetaxel (75 mg/m²) was given once every 3 weeks for six cycles, with prednisolone/prednisone (10 mg) daily. On the AAP arm, abiraterone acetate (1000 mg) with prednisolone/prednisone (5 mg) daily was given until PSA, clinical and radiological progression or a change of treatment. AAP duration was capped at 2 years in M0 patients having radical radiotherapy. Modifications for toxicities were described in the protocol and previous papers [7, 10]. Treatment allocation was not masked for practical reasons. Patients were seen 6-weekly at first, dropping to 6-monthly after 2 years. Imaging scans after baseline were at the investigator’s discretion.

Randomisation

Patients were randomised centrally using minimisation with a random element across a number of stratification factors using unequal allocation (previously described) [7, 10]. The allocation ratio was initially 2 : 1 control : research; the ‘abiraterone comparison’ was brought in with an equal allocation (1 : 1) ratio to the control. Therefore the allocation ratio here is 1 : 2 for SOC + DocP : SOC + AAP.

Statistical analysis

The comparison presented here is of SOC + AAP against SOC + DocP because both of these arms have demonstrated better OS than their contemporaneous controls in the population of men starting long-term hormone therapy. The protocol specified that research arms which were better than the control arm could be compared, following a closed test approach. The maturity of the data used for SOC + AAP matches that recently reported [10] in the primary results and is updated to the same data freeze timepoint for SOC + DocP so is longer-term data than previously reported results for this arm [7].

The previously-reported comparisons of SOC + DocP versus SOC and SOC + AAP versus SOC had formal sample size calculations; there is no formal sample size calculation for this comparison: it is an opportunistic comparison between the contemporaneously recruited research arm patients. Although the recruitment overlap is only 17 months, 566 patients were allocated to the 2 research arms of interest and thus contribute substantial information to inform this comparison.

Standard survival analysis methods were used, following the approach for each of these underpinning comparisons; hazard ratios (HR) were estimated from adjusted Cox models, after checking that the proportional hazards assumption held, where an HR < 1 represents evidence in favour of SOC + AAP and HR > 1 represents evidence in favour of SOC + DocP. Nominal confidence intervals are presented at the 95% level. A P-value <0.1 was considered indicative of treatment-baseline characteristic interaction, recognising the limited power of the heterogeneity tests. Efficacy analyses were done in the intention-to-treatment basis, by allocated treatment. Safety analyses were done only in patients who started their allocated treatment.

Results

Accrual and characteristics

The dataset for this comparison was frozen on 10 February 2017. Between 15 November 2011 and 31 March 2013, 1348 patients joined all open arms STAMPEDE. Of the 566 randomised to the comparison reported here, 189 (14%) were allocated to SOC + DocP, 377 (28%) to SOC + AAP. The flow of patients to this comparison is shown in Figure 2. Table 1 shows the baseline characteristics of patients in this comparison which differ only slightly from the previous papers (summarised in supplementary Table S1, available at Annals of Oncology online). Median follow-up, calculated by reverse censoring on survival, was 48 months.

Overall survival

There were 44/189 (23%) deaths on the SOC + DocP arm and 105/377 (28%) deaths on the SOC + AAP arm. The estimated HR = 1.16 (95% CI 0.82–1.65; P = 0.40) (Figure 3A). Estimates in patients with and without metastases are shown in Table 2, with HR = 1.51 (95% CI 0.58–3.93) in M0 patients and HR = 1.13 (95% CI 0.77–1.66) in M1 patients. There was no evidence of interaction in the treatment effect by baseline metastases (P = 0.69).

Totally, 126/149 deaths were attributed to prostate cancer, comprising 10/22 and 116/127 deaths in patients with M0 and M1 disease at entry, respectively. Competing risks regression shows no evidence of a difference in prostate cancer-specific
Figure 1. Activity-by-time diagram: patients included in this comparison. SOC, standard-of-care; Doc, docetaxel; Abi, abiraterone acetate-prednisolone/prednisone. Boxes represents periods of recruitment (x-axis) to each of the trial arms (y-axis). The blue boxes represent recruitment periods contributing to this analysis; the green boxes other recruitment period, past and future, contributing to other aspects of the STAMPEDE. The squares represent the time point of the first key comparative analyses for each comparison in pink and for this comparison in blue.

Figure 2. CONSORT diagram. SOC, standard-of-care; DocP, docetaxel-prednisolone/prednisone; AAP, abiraterone acetate-prednisolone/prednisone. Selection of patients for this comparison.
Table 1. Baseline characteristics of patients allocated to SOC + DocP or SOC + AAP by whether contributing to the direct comparison

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survival (sub-HR = 1.02, 95% CI 0.70–1.49). For non-prostate cancer-specific survival, with 23/149 deaths attributed to other causes, the sub-HR was 2.33 (95% CI 0.78–6.99). There was no evidence of heterogeneity of treatment effect by baseline metastases in either outcome.

Other efficacy OMs

Table 2 shows the effect size overall and by whether the patients had metastases at entry for FFS, PFS, MPFS and skeletal-related events. There is no evidence of heterogeneity of the treatment
effect by baseline metastases in any of these OMs. Figure 4 summarises the effect for all OMs.

**Safety**

The safety population includes people who started their allocated treatment. While nearly all patients allocated to AAP started it, a proportion of those patients allocated to receive docetaxel declined to start it. Table 3 summarises the worst toxicity reported for patients over their time on trial in the safety population and shows differing patterns for adverse events according to treatment. The prevalence of grade 3 or 4 toxicity in patients with assessments at 1 year without a prior FFS event was 11% SOC + DocP and 11% SOC + AAP; at 2 years this was 11% SOC + DocP and 11% SOC + AAP.

**Second-line treatment**

Figure 5 shows time from randomisation to any subsequent exposure to docetaxel or AR-targeted therapy with AAP or enzalutamide. Figure 6 shows time from an FFS event to reported exposure to selected treatments that are licensed for CRPC: docetaxel, AAP, enzalutamide. There was limited reported use of cabazitaxel, radium and sipuleucel-T at this point (not shown).
Discussion

We and others have previously shown a survival advantage for adding docetaxel (with or without prednisolone/prednisone) and for adding abiraterone acetate and prednisolone/prednisone, in patients starting long-term hormone therapy for the first time [4–11]. However, there is currently no direct evidence available to help clinicians or patients assess which combination might be better. Here, we reported a pre-specified (but not pre-powered) analysis using only patients who were randomised during a period of the study when recruitment to the two research arms overlapped. We used data collected prospectively from over 100 sites across two countries as part of a clinical trial protocol. The MAMS platform design of STAMPEDE, an approach sometimes referred to as a master protocol [16], facilitated this comparison. Separate, traditional, two-arm RCTs, would not have allowed any directly randomised comparative evidence to be available so soon.

Our recently reported overall treatment effect on survival, in STAMPEDE, for adding AAP compared with the SOC (HR = 0.63) [10] was larger than the previously-reported overall treatment effect, in STAMPEDE, on survival for adding DocP to the same SOC (HR = 0.78) [7]. The earlier secondary efficacy OMs favoured adding AAP over DocP, including FFS—perhaps unsurprising given the direct antiandrogenic action of AAP (around four in every five FFS events was driven only by a rise in PSA) and PFS (which excludes rising PSA). There was weak evidence favouring AAP for MPFS and no evidence of a difference in symptomatic skeletal events, prostate cancer-specific survival or OS.

Comparing the results indirectly of these two therapies by readers extracting data from STAMPEDE’s AAP and docetaxel papers [7, 10] may not be the most appropriate way to compare the relative effectiveness: the patient cohorts were all not randomised contemporaneously and there may be confounding biases when comparing the two datasets, in particular, many DocP patients had very limited salvage CRPC options compared with AAP patients, simply due to the timing of licences of new therapies (see below).

Importantly, the two therapies are being used in different ways. AAP is used until the patient has castrate-resistant prostate cancer (CRPC), often lasting many years and consequently exhausting a major therapy option for CRPC. In contrast, DocP is given as an 18-week course thus all CRPC options should remain available. Our data reveal important differences in the pattern of treatment failure yet we do not see any differences in survival, suggesting that the relative time spent before and after first-line treatment failure are quite different by initial treatment. This may explain why the early, often biochemically driven OMs, favour AAP but the later post CRPC end points such as skeletal events, prostate cancer-specific survival and OS show no good evidence of a difference. Men receiving DocP will thus spend longer with CRPC than men receiving AAP but with a broader range of more effective options available. Supplementary Figure S1, available at

Table 3. Worst adverse event (grade) reported over entire time on trial

<table>
<thead>
<tr>
<th>Safety population</th>
<th>SOC + Doc (n = 189)</th>
<th>SOC + AAP (n = 377)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients included in analysis</td>
<td>172</td>
<td>373</td>
</tr>
<tr>
<td>Patients with an adverse event—no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1–5 adverse event</td>
<td>172 (100)</td>
<td>370 (99)</td>
</tr>
<tr>
<td>Grade 3–5 adverse event</td>
<td>86 (50)</td>
<td>180 (48)</td>
</tr>
<tr>
<td>Grade 3–5 adverse events—no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine disorder</td>
<td>15 (9)</td>
<td>49 (13)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>29 (17)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Neutropenia (neutrophils)</td>
<td>22 (13)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>General disorder</td>
<td>18 (10)</td>
<td>21 (6)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (4)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Oedema</td>
<td>1 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Musculoskeletal disorder</td>
<td>9 (5)</td>
<td>33 (9)</td>
</tr>
<tr>
<td>Cardiovascular disorder</td>
<td>6 (3)</td>
<td>32 (9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0 (0)</td>
<td>12 (3)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (1)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Cardiac dysrhythmia</td>
<td>1 (1)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>9 (5)</td>
<td>28 (8)</td>
</tr>
<tr>
<td>Hepatic disorder</td>
<td>1 (1)</td>
<td>32 (9)</td>
</tr>
<tr>
<td>Increased AST</td>
<td>0 (0)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>1 (1)</td>
<td>23 (6)</td>
</tr>
<tr>
<td>Respiratory disorder</td>
<td>12 (7)</td>
<td>11 (3)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>4 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>5 (3)</td>
<td>20 (5)</td>
</tr>
<tr>
<td>Lab abnormalities</td>
<td>9 (5)</td>
<td>11 (3)</td>
</tr>
<tr>
<td>Hypokalaemia</td>
<td>0 (0)</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

*aThe safety population includes patients who started their allocated treatment.

Figure 4. Depiction of disease state over time.
Figure 5. Time from randomisation to reported starting docetaxel, AAP, enzalutamide or AR-targeting therapy. Kaplan–Meier (survival) plots showing cumulative incidence of exposure to treatments after randomisation. Each step up the y-axis represents an event, namely starting that particular treatment. The number of patients contributing information (at risk) over time since randomisation is shown under the table. The number of patients with an event between these points is shown in brackets. For example, in Figure 4C between 24 and 36 months after randomisation, 4 patients on the SOC+DocP arm report starting abiraterone and (150/129—4 are 17 are censored and may start in the future.

Figure 6. Time from failure-free survival event to subsequent treatment by allocated treatment. Kaplan–Meier (survival) plots showing cumulative incidence of exposure to treatments after a failure-free survival (FFS) event. Doc, docetaxel; AAP, abiraterone acetate + prednisolone; Enz, enzalutamide. Each step up the y-axis represents an event, namely starting that particular treatment.
and sipuleucel-T although not widely accessible in any realistic differences. The trigger for the analysis was the re-
not designed in the usual way, hence power is limited to detect effect sizes.
practice; but the lack of compliance with allocated treatment of may change future compliance with both treatments in routine
12 patients did not start their allocated docetaxel. Our results
arms and very similar to our previous estimate for SOC. Nearly for these agents (Table 3). In patients who started their allocated
toxicity was similar and in line with previously reported toxicities
to-event analyses. The number of patients with metastases at baseline was balanced by arm, but, particularly because of their poorer prognosis, these patients tend to predominate in this analysis. There is no evidence of heterogeneity in the treatment effect by baseline metastasis for any of the OMs, but power to detect any heterogeneity is very limited, especially in later OMs with fewer events.
The patterns of toxicity are quite different for the two treatment
approaches, consistent with the known effects of the drugs. The proportion of patients reporting at least one grade 3 or worse toxicity was similar and in line with previously reported toxicities for these agents (Table 3). In patients who started their allocated treatment and who are without disease progression at 1 year, the prevalence of grade 3 or worse toxicity was about 11% on both arms and very similar to our previous estimate for SOC. Nearly all patients started their allocated abiraterone, whereas about 1 in 12 patients did not start their allocated docetaxel. Our results may change future compliance with both treatments in routine practice; but the lack of compliance with allocated treatment of docetaxel is likely to have had some impact on our estimated ef-
effects.
A key limitation is that the comparison was opportunistic and not designed in the usual way, hence power is limited to detect any realistic differences. The trigger for the analysis was the re-
porting of our ‘abiraterone comparison’ data [10]. The unequal allocation ratio reflects the planned design of the comparisons. The allocated treatment being given was not masked for practical reasons. This, of course, allowed for relapse therapies to be given at the investigator’s discretion. We observed that after relapse, many patients received the treatment class that they had not received up-front.
Salvage options have changed over time: men recruited earlier on to DocP (2005–2013) will have had very different options to those recruited later to AAP (2011–2014) when there were more CRPC therapies likely available, including AAP [17, 18], cabazitaxel [19], docetaxel [20, 21], enzalutamide [22, 23], radium-223 [24] and sipuleucel-T [25] (although not widely accessible in
Europe). For this analysis, we limited ourselves to patients contemporaneously randomised to either arm to make this compar-
sion as fair as possible. However, FFS events generally happened sooner with DocP than with AAP in time from randomisation and, therefore, calendar year (Table 4) may partially influence outcomes. Furthermore, a FFS event was more of an indication to change treatments on DocP; AAP continued beyond this point.
As far as we are aware there are no ongoing randomised trials directly comparing adding AAP versus adding docetaxel for patients starting long-term ADT. All of our published STAMPEDE data have contributed to the STOPCaP aggregate data network meta-analysis that has used all of the reported RCTs in metastatic patients to perform indirect comparisons and allow some assessment of potential ranking of effective therapies. This aggregate data analysis (co-submitted) will be supplemented by a forthcoming individual patient data (IPD) network meta-analysis which will hopefully provide a more accurate reflection of the temporal interval between the application of the two different therapies, to which STAMPEDE will contribute all relevant data. We will continue to follow-up pa-
tients for long-term OMs.
Considering their mechanisms of action and their proven oncological benefits, the question is raised of whether a combin-
uation of AAP plus docetaxel might lead to an approximately addi-
tive benefit of using them both, further extending survival. Randomised data on docetaxel with or without abiraterone will emerge from a subset the PEACE-1 trial (https://clinicaltrials. gov/ct2/show/NCT01957436), as will non-randomised, time-
stratified data on abiraterone with or without docetaxel. Similarly comparative data will also emerge for enzalutamide, an-
other AR-targeted therapy, from the ENZAMET trial (https://clin
icaltrials.gov/ct2/show/NCT02446405) and with the combin-
ation of enzalutamide and AAP in STAMPEDE (Figure 1).
In conclusion, there are now two systemic therapies, DocP and AAP, which have shown a survival benefit from RCTs when added to treatment of patients starting long-term ADT for the first time. The evidence from our directly randomised data compar-
ing these two therapies showed no evidence of a difference in overall or prostate cancer-specific survival, nor in other import-
ant outcomes such as symptomatic skeletal events, suggesting that both currently remain viable new standards-of-care.

<table>
<thead>
<tr>
<th>Year of event</th>
<th>FFS event</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SOC + DocP</td>
<td>SOC + AAP</td>
</tr>
<tr>
<td>2012</td>
<td>14 7</td>
<td>25 6</td>
</tr>
<tr>
<td>2013</td>
<td>38 20</td>
<td>43 11</td>
</tr>
<tr>
<td>2014</td>
<td>25 13</td>
<td>33 9</td>
</tr>
<tr>
<td>2015</td>
<td>14 7</td>
<td>11 3</td>
</tr>
<tr>
<td>2016</td>
<td>6 3</td>
<td>10 3</td>
</tr>
<tr>
<td>No event</td>
<td>92 49</td>
<td>255 68</td>
</tr>
</tbody>
</table>
UK

- Aberystwyth, Bronglais General Hospital (4: Porfiri; Durrani)
- Ashford William Harvey Hospital (19: Thomas; Mithal)
- Aylesbury, Stoke Mandeville Hospital (14: Sabharwal; Camilleri)
- Ayr Hospital (54: Glen; Ansari)
- Barnet General Hospital (25: McGovern; Eichholz)
- Basingstoke & N Hampshire Hospital (21: Shaffer)
- Bath, Royal united Hospital (70: Frim; Beresford)
- Belfast City (191: O’Sullivan; Mitchell, Stewart, Shum)
- Birmingham, City Hospital (26: Sivoglo; Ford)
- Birmingham, Good Hope Hospital (18: Ford)
- Birmingham, Heartlands Hospital (38: Zarkar)
- Birmingham, QE (180: James; Porfiri, Ford)
- Blackburn East Lancashire Trust (180: Parikh; Charnley)
- Bolton, Royal Bolton Hospital (30: Elliott, Maddineni)
- Boston, Pilgrim Hospital (38: Sreenivasan; Panades)
- Bournemouth, Royal Bournemouth Hospital (100: Brock)
- Bradford Royal Infirmary (36: Brown)
- Brighton, Royal Sussex County Hospital (92: Robinson; Robinson, Bloomfield)
- Bristol Haematology & Oncology Centre (106: Bahl; Herbert, Masson)
- Burton, Queen’s Hospital (108: Smith-Howell; Chetiyawardana, Pattu)
- Bury St Edmunds, West Suffolk Hospital (21: Woodward)
- Cardiff, Velindre (341: Lester; Staffurth, Barber, Kumar, Panaliappan, Button, Tanguay)
- Chelmsford, Broomfield Hospital (88: Hamid; Panwar, Leone)
- Cheltenham General Hospital (54: Bowen)
- Chester, Countess of Chester Hospital (79: Ibrahim)
- Coventry & Warwickshire, University Hospital (40: Worling; Stockdale)
- Crewe & Nantwich, University Hospital (54: Wylie)
- Cumbria, Cumberland Infirmary (18: Kumar)
- Darlington Memorial Hospital (49: Kagzi; Hardman, Peedell)
- Derby, Royal Derby Hospital (130: Chakraborti; Pattu)
- Devon, North Devon District Hospital (33: Sheehan)
- Doncaster Royal Infirmary (35: Bowen; Ferguson)
- Dorset County Hospital (30: Crellin; Afzal, Andrews)
- Dudley, Russells Hall Hospital (81: Keng-Koh; Ramachandra)
- Durham University Hospital (17: Heath; McMenemin)
- Eastbourne District General Hospital (63: McKinna)
- Edinburgh, Western General (112: McLaren)
- Essex County Hospital (58: Muthukumar; Sizer, Kumar)
- Exeter, Royal Devon & Exeter (189: Sheehan; Sreenivasan)
- Gillingham, Medway Hospital (29: Kumar; Taylor)
- Glasgow, Beatson West of Scotland Cancer Centre (323: Graham; Venugopal, Wallace, Jones, Lamb, Glen, Russell)
- Guildford, Royal Surrey County Hospital (132: Laing; Khakhsar, Wood, Money-Kytle)
- Harlow, Princess Alexandra Hospital (54: Gupta; Melcher, Melcher)
- Hereford County Hospital (71: Grant; Cook)
- Huddersfield Royal Infirmary (105: Hofmann)
- Hull, Castle Hill Hospital (119: Simms; Hetherington)
- Inverness, Raigmore Hospital (88: McPhail; MacGregor)
- Ipswich Hospital (103: Brierly; Venkitaraman, Scrase)
- Keighley, Airedale Hospital (52: Brown; Crawford)
- Kent and Canterbury Hospital (79: Thomas; Raman, Mithal, Malde)
- Kent, Queen Elizabeth Queen Mother Hospital (27: Thomas; Raman)
- Kidderminster General Hospital (40: Capaldi; Churn)
- Larbert, Forth Valley Royal Hospital (36: Sidek)
- Leeds, St James University Hospital (94: Cross; Loughrey, Bottomley, Prescott)
- Lincoln County Hospital (50: Sreenivasan; Ballesteros-Quintail, Panades, Baria)
- Liverpool, Royal Liverpool University Hospital (88: Malik; Robson, Esvar)
- Liverpool, University Hospital Aintree (26: Robson)
- London, Charing Cross Hospital (38: Falconer; Mangar)
- London, Guy’s Hospital (161: Choudhury)
- London, Hammersmith Hospital (4: Falconer; Mangar)
- London, North Middlesex Hospital (24: Gupta; Newby, Thompson)
- London, Royal Free Hospital (44: Vilarino-Varela; Pigott)
- London, St Georges Hospital (35: Pickering)
- London, St Mary’s Hospital (8: Falconer; Stewart)
- London, University College Hospital (46: McGovern)
- Maidstone, Kent Oncology Centre (114: Beesley)
- Manchester Christie Hospital (167: Clarke; Elliott, Livsey, Choudhury, Wylie)
- Manchester Hope Hospital (59: Clarke; Elliott, Lau, Tran)
- Manchester, Royal Oldham Hospital (54: Conroy; Livsey, Choudhury)
- Manchester, Withington Hospital (7: Sangar)
- Middlesbrough, James Cook UH (103: Peedell; Van der Voet, Hardman, Shakespeare)
- Newcastle, Freeman Hospital (92: Azzabi; McMenemin, Frew)
- North Staffordshire UH (80: Adab)
- Northwood, Mount Vernon Hospital (126: Hoskin; Anyamene, Ostler, Alonzi)
- Nottingham University Hospitals (City Campus) (141: Sundar; Mills)
- Nuneaton, George Eliot Hospital (14: Khan; Chan)
- Oxford, Churchill Hospital (165: Protheroe; Cole, Sabharwal, Sugden)
- Poole Hospital (62: Davies)
- Portsmouth, Q Alexandra Hospital (173: Gale)
- Preston, Royal Preston Hospital (221: Birtle; Parikh, Wise)
- Reading, Royal Berkshire Hospital (42: Rogers; O’Donnell, Brown, Brown)
- Redditch, Alexandra Hospital (15: Capaldi; Hamilton)
- Romford, Queen’s Hospital (127: Gibbs; Subramaniam)
- Scarborough General Hospital (82: Hingorani)
- Sheffield, Weston Park (142: Ferguson)
- Shrewsbury, Royal Shrewsbury Hospital (192: Srinari)
- Somerset, Weston General Hospital (18: Hilman)
• Southampton General Hospital (75: Jones; Heath, Wheater, Crabb)
• Southend University Hospital (114: Tsang; Ahmed, Chan)
• Southport and Formby District GH (46: Bhalla; Sivapalasuntharam, Sivapalasuntharam)
• St Leonards-on-Sea, Conquest Hospital (42: McKinna; Beesley, Lees)
• Stevenage, Lister Hospital (35: Hughes)
• Stockport, Stepping Hill Hospital (106: Logue; Coyle)
• Stockton-on-Tees, UH North Tees (28: Leaning; Shakespeare)
• Sunderland Royal Hospital (45: Azzabi)
• Sutton-in-Ashford, King’s Mill Hospital (64: Saunders)
• Sutton and London, Royal Marsden Hospital (162: Dearnaley; Parker, Selvadurai)
• Swansea, Singleton (188: Wagstaff; Phan, Phan)
• Swindon, Great Western Hospital (52: Khan; Cole)
• Taunton, Musgrove Park Hospital (137: Gray; Graham, Varughese, Plataniotis)
• Torbay District General Hospital (135: Lydon; Srinivasan)
• Tyne & Wear, S Tyneside District Hospital (6: Azzabi)
• Warrington Hospital (111: Syndikus; Tolan)
• Warwick Hospital (17: Chan; Stockdale)
• Wigan, Royal Albert Edward Infirmary (37: Tran)
• Wirral, The Clatterbridge Cancer Centre NHS Foundation Trust (128: Tolan; Syndikus, Ibrahim, Montazeri, Littler)
• Wolverhampton, New Cross Hospital (53: Gray; Sayers)
• Woolwich, Queen Elizabeth Hospital (18: Hughes)
• Worcestershire Royal Hospital (57: Capaldi; Bowen)
• Worthing Hospital (90: Nikapota)
• Wycombe Hospital (52: Sabharwal; Protheroe, Pwint)

Switzerland
• Basel Universitätsklinikum (5: Rentsch)
• Berne University Hospital (Inselspital) (5: Thalmann)
• Chur Kantonsspital Graubunden (31: Strebel; Cathomas)
• Kantonsspital St Gallen (10: Engeler)
• Lausanne, Centre Hospital Univ Vaudois (7: Berthold; Jichlinski)

Plus more than 3000 local site team staff across these hospitals.

Trials Unit Staff (from 2011 onwards)

MRC Clinical Trials Unit at UCL

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Tim Smith, Jacque Millet, Shama Hassan, Philip Pollock, Richard Gracie, Laura Van Dyck, Charlene Green, Elizabeth Clark, Sara Peres, Hannah Gardner, Dominic Hague, Katie Ward, Peter Vaughan, Eva Ades, Hannah Babiker, Zohrah Khan, Nargis Begum, Saba Khan, Jenna Grabey

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• Clinicians—Clare Gilson, Alastair Ritchie; Previously—Sarah Meredith, Ruth Langley
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Swiss Group for Cancer Clinical Research

• Project and Trial Managers—Corinne Schar; Previously—Estelle Cassol
• Patient and Public Involvement representatives—David Matheson, Robin Millman

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References


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