Barts ECMC - ECMC Annual Network Meeting 2019

Centre Overview & Achievements

Two sub-teams: one for the management of investigator led and sponsored trials and one patient facing for the delivery of externally sponsored trials.

Clinical Trials Team

National/ international oversight
Protocol development
Regulatory submissions
Pharmacovigilance
Monitoring

Protocol design
Statistical analysis
Clinical study reports
Publications

Biological sample centralisation

Bespoke eCRF
IWRS

Support Across Both Teams

Oversight of IMP aspects
Technical expertise
Specialist operational advice

Quality and compliance
QMS
Audits

Centre Administration
Finance

Trial Delivery Team

Patient recruitment
Data collection

Hosted study set up
Amendment administration

- Three investigator led and sponsored trials presented as oral abstracts at large international oncology conferences:
  - ABACUS, Powles T et al ASCO 2018 [1]
  - PAKT, Schmid P et al ASCO 2018 [2]
  - CALYPSO, Powles T et al ASCO GU 2019 [3]
- Positive results of the PAKT trial (Ph II in TNBC) led to a phase III trial led by Prof Schmid.
- Positive results of STAR_PAC trial (Ph I in pancreatic cancer) led to a phase II trial led by Prof H. Kocher.
- Barts recruited the first patient globally in 5 clinical trials.
- Barts was the highest recruiter globally in 4 trials.
- Recruiting centre for personalised cancer vaccine clinical trials.
- Barts Investigators were leading authors/presenters for 4 trials:
  - Keynote-426 (Powles T): ASCO GU2019 presentation & NEJM publication.[4]
  - Impassion-130 (Schmid P): ESMO 2018 Presidential Symposium & NEJM publication.[5] Study led to FDA and EMA approval.
  - AUGMENT (Gribben J) JCO publication.[6] The results of this trial led to filing for approval for lenalidomide in low grade non- Hodgkin's lymphoma.
  - TRAP (Szlosarek P) Clin Cancer Res [7]
  - Lead authors in Nature (Powles T)[8] and JAMA (Schmid)[10] publications investigating molecular correlates of response in renal and triple negative breast cancer respectively.

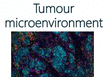
Immunotherapy Centre

Immunotherapy Centre
1 of 26 centres from 10 countries to be part of the imCORE (Immunotherapy Centre of Research Excellence) Network

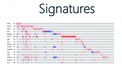
Biomarker driven investigator led trials
Tissue resource of paired bladder and breast tumour tissue samples (pre- and post-immunotherapy)

Established collaborations with international labs investigating the effects of immunotherapy on:

Tumour microenvironment



Genetic Signatures



Microbiome

ABACUS: Neoadjuvant immunotherapy in MIBC [1]

Open-label, international, multicentre phase II trial. Sponsored by QMUL and managed by the Barts ECMC Trials Team (Fig. 1).

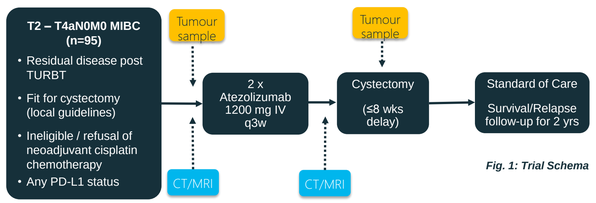


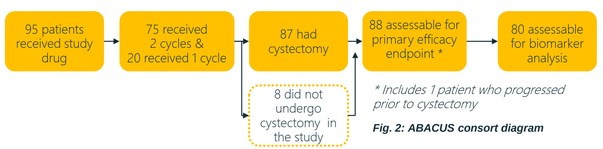
Fig. 1: Trial Schema

Primary endpoints: pCR (clinical) and changes in PAN-CK CD8 expression in tumour samples pre- and post atezolizumab treatment (biological)

Secondary endpoints: RR, DFS, Safety, Surgical complications (Clavien – Dindo) & OS

Data cutoff: 10 DEC 2018; **Median Follow-up:** 13.1 months (95%CI: 9.5 – 13.5)

From May 2016 to June 2018, 121 patients were screened in 21 sites from 4 EU countries (Fig. 2).



** Includes 1 patient who progressed prior to cystectomy*

Fig. 2: ABACUS consort diagram

- The study met its primary endpoint with a pCR of 31% (27/88) [95%CI:21%-41%] (Fig3.)
- CD8 infiltration occurred in 71% of pCR samples, remainder were characterised by fibrosis.
- 12-month relapse-free survival was 74% [95%CI: 62-83%].

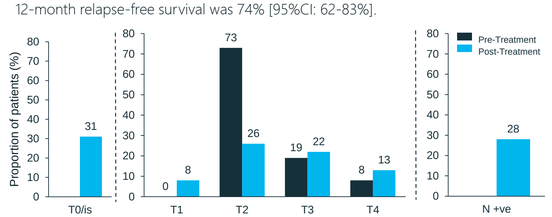


Fig. 3: Change in T and N stage associated with therapy. Pre-treatment assessment by TURBT pathology and cross sectional imaging (n=95). Post-treatment assessment by cystectomy pathology and lymphadenectomy.

Fig 4: 35/88 (40%) patients were PD-L1+ve at baseline (IC staining of ≥5% with SP142 antibody) with a pCR rate of 37% [95%CI:22%-55%] and a 1 year relapse free survival of 75% [95%CI: 53% - 87%].

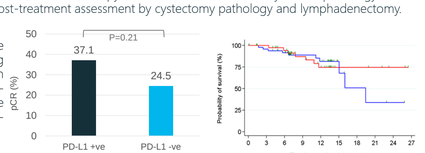
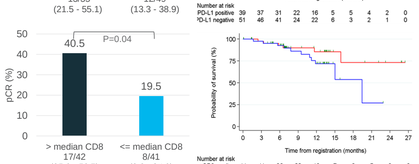


Fig 5: Tumours with CD8 results (n=83) were dichotomised above and below the median count at baseline. pCR rate for CD8 high was 41% (95%CI: 26-57%) and 1 year relapse free survival was 85% (95%CI: 67 - 94%).



PAKT: AKT inhibition + chemotherapy in 1L metastatic TNBC [2]

International, multicentre, blinded randomised phase II trial. Sponsored by QMUL and managed by the Barts ECMC Trials Team (Fig. 6).

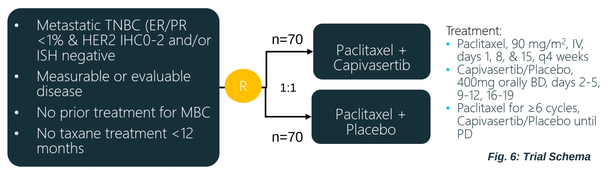


Fig. 6: Trial Schema

Stratification factors: Number of metastatic sites (<3, ≥3) & DFI (end of (neo)adjuvant chemotherapy ≤12 months ago, end of (neo)adjuvant) chemotherapy >12 months or no prior chemotherapy)

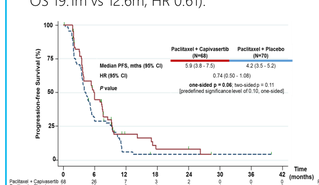
Primary endpoint: Investigator assessed PFS (ITT)

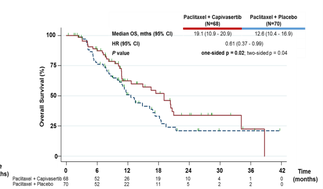
Secondary endpoints: PFS in patients with/without *PIK3CA/AKT1/PTEN* alterations, OS, ORR, CBR, DoR, Safety

Data cutoff: 22Jan2018; **Median Follow-up:** 18.2 months (95%CI, 13.5-24.0)

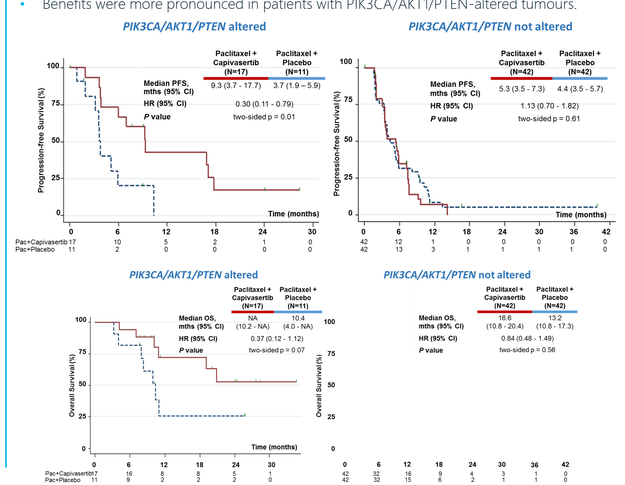
From May 2014 to June 2017, 175 patients were screened and 140 randomised from 42 sites in 6 countries (UK, FR, HU, SKR, RO, GEO).

- Addition of the AKT inhibitor Capivasertib to 1L paclitaxel therapy for TNBC resulted in significantly longer PFS (median PFS 5.9m vs 4.2m; HR 0.74).
- Addition of Capivasertib was associated with a significantly longer overall survival (median OS 19.1m vs 12.6m; HR 0.61).





- Benefits were more pronounced in patients with PIK3CA/AKT1/PTEN-altered tumours.



CALYPSO: cMET inhibition + immunotherapy in metastatic papillary RCC[3]

Open-label, international, multicentre phase II trial. Sponsored by QMUL and managed by the Barts ECMC Trials Team (Fig. 7).

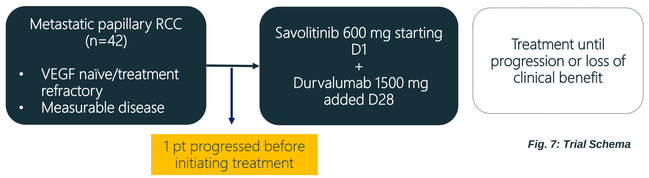


Fig. 7: Trial Schema

Primary endpoint: ORR

Secondary endpoints: PFS, OS, DoR, Duration of response, Best response 24wks, Safety

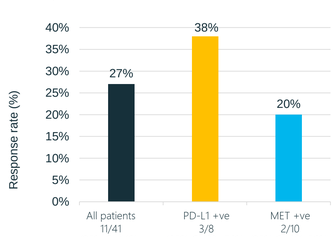
Data cutoff: 25Sep2018; **Median follow-up:** 6.9 months (95% CI: 4.7 – 10.0)

- Combination of savolitinib and durvalumab was associated with durable responses in papillary RCC.
- Initial Sequencing of the drugs may have had an effect on efficacy.
- The combination was tolerable with nausea, fatigue and oedema being most prominent AEs.

Best overall response	All patients (N=41) n (%)	All patients (N=41) 95% CI for %	Previously untreated (N=28) n (%)	Previously untreated (N=28) 95% CI for %
PR	11 (27)	(14 - 43)	9 (32)	(16 - 52)
SD	16 (39)	(24 - 55)	12 (43)	(24 - 63)
PD	11 (27)	(14 - 43)	5 (18)	(6 – 37)
NA*	3 (7)	(2 – 20)	2 (7)	(1 – 24)

- PD-L1 and MET biomarker expression did not clearly correlate with outcome.

Best overall response	PD-L1+ (N=8) n (%)	MET+ (N=10) n (%)
PR	3 (38)	2 (20)
SD	1 (13)	5 (50)
PD	3 (38)	2 (20)
NA*	1 (13)	1 (10)



*Only baseline scan available.

- 8/41 PD-L1 +ve (>25% immune component with SP263 Ab). 27 PD-L1-ve.
- 10/41 patients MET +ve (≥ 3+ in ≥ 50% tumour cells with IHC). 25 MET -ve.
- 6 patients not assessable/available for both biomarkers.

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