55 The introduction of the Cancer Research UK Stratified Medicine Programme 2 (CRUK SMP2) in North East England; lessons learned and experience gained

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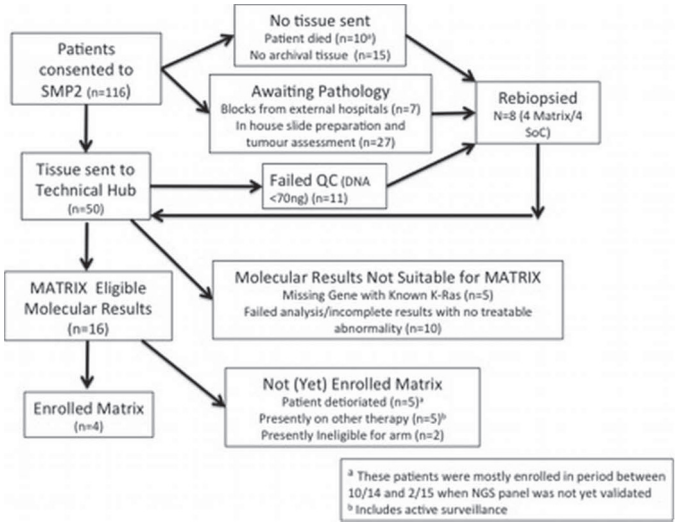
Introduction: The CRUK SMP2 programme was set-up to evaluate the feasibility of performing large scale molecular analysis within the NHS on the (often small) diagnostic biopsies obtained in NSCLC. The results are used to allocate patients to an appropriate molecular therapy within the "umbrella" MATRIX trial. Newcastle opened SMP2 on 01/10/2014. Here we report our first year's experience.
Methods: NSCLC patients with PS 0–2 were consented onto the CRUK SMP2. Matched residual diagnostic tissue and blood were sent to All Wales Genetics Laboratory, Cardiff. Samples with >70ng DNA were assessed for 28 oncogenes using Next Genuine Sequencing on the Illumina SMP2 panel.
Results: 116 patients were consented from 6/10/14–1/10/15 referred from 12 oncologists. The data on patient/sample flow is shown in Fig 1. Median survival was 161 days from consent. The 1st sample was sent to Cardiff on 28/1/15 as the Illumina panel was undergoing final validation. 50 samples have been sent; 11 had insufficient DNA; these samples had lower cell number (but with no impact of necrosis/tumour proportion); The most commonly altered gene was K-Ras (13 of 22 adenocarcinomas). Only 2 patients with results from >25 of the 28 genes had no tier 1 or 2 ie potentially treatable molecular abnormalities. The median time from consent to result was 109 days (range 45–250) with delays occurring throughout the pathway.



Conclusion: Patients and oncologists are keen to be involved in molecular profiling; but patients need to be consented early to allow results to guide therapy. Prioritisation of samples is key. Not all samples are suitable for analysis due to small cell number or low tumour proportion. Molecular analysis may require extra resource in pathology, if it is to become standard of care. The first 4 patients to start treatment on MATRIX were enrolled from 27/8/15 in Newcastle.
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56 Efficacy and safety of brigatinib (AP26113) in ALK+ NSCLC: phase 1/2 trial results

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Introduction: Brigatinib is an investigational oral tyrosine kinase inhibitor with preclinical activity against both rearranged ALK and clinically identified crizotinib-resistant mutant ALK.
Methods: In this ongoing phase 1/2, single-arm, open-label, multicenter study in patients with advanced malignancies (N=137; NCT01449461), patients received oral brigatinib at total doses of 30–300 mg daily. Antitumor efficacy (per RECIST v1.1) and safety data are reported in ALK+ NSCLC and all patients, respectively.
Results: Median age of ALK+ NSCLC patients (n=79) was 54 (29–83) years, 49% were female, 90% received prior crizotinib, and 47% had ≥2 prior chemotherapy regimens. As of February 17, 2015, 45/79 (57%) remained on study; median time on treatment was 12.6 months (1 day to 35.5 months). Evaluable ALK+ NSCLC patients had ORR/median PFS of 74%/13.4 months (Table). A post hoc independent radiological review of patients with brain metastases at baseline showed (as of February 9, 2015): 8/15 (53%) patients with measurable brain lesions ≥10 mm had an intracranial response; 11/31 (35%) patients with only nonmeasurable lesions had disappearance of all lesions. Treatment-emergent AEs in ≥30% of total patients (N=137), generally grades 1/2, included nausea (52%), fatigue (42%), diarrhea (40%), headache (33%), and cough (32%); serious AEs in ≥2% of all patients, regardless of attribution, included dyspnea (7%), pneumonia (6%), hypoxia (5%), pulmonary embolism (3%), and pyrexia (2%).

Response and PFS in Evaluable Patients With ALK+ NSCLC Treated With Brigatinib

Endpoint	All n=78	Prior Crizotinib n=70	No Prior Crizotinib n=8
Response, n (%)			
OR (CR + PR)	58 (74)	50 (71)	8 (100)
[95% CI]	[63–84]	[59–82]	[63–100]
CR	7 (9)	4 (6)	3 (38)
PR	51 (65)	46 (66)	5 (63)
SD	11 (14)[a]	11 (16)[a]	0
PD	6 (8)	6 (9)	0
Termination before scan	3 (4)	3 (4)	0
Median duration of response,[b] mo	11.2	9.9	Not reached
Median PFS,[b] mo	13.4	13.4	Not reached

[a] Includes non-CR/non-PD for 4 patients with no measurable disease at baseline
[b] Based on Kaplan-Meier estimate; 55 patients were evaluable for duration of response, 48 with prior crizotinib and 7 with no prior crizotinib

Conclusion: Brigatinib had antitumor activity in ALK+ NSCLC patients with (71% ORR; median PFS, 13.4 months) or without (100% ORR) prior crizotinib, including patients with brain metastases (53% ORR, measurable brain lesions). A pivotal, randomized, phase 2 trial of brigatinib in patients with crizotinib-resistant ALK+ NSCLC is on-