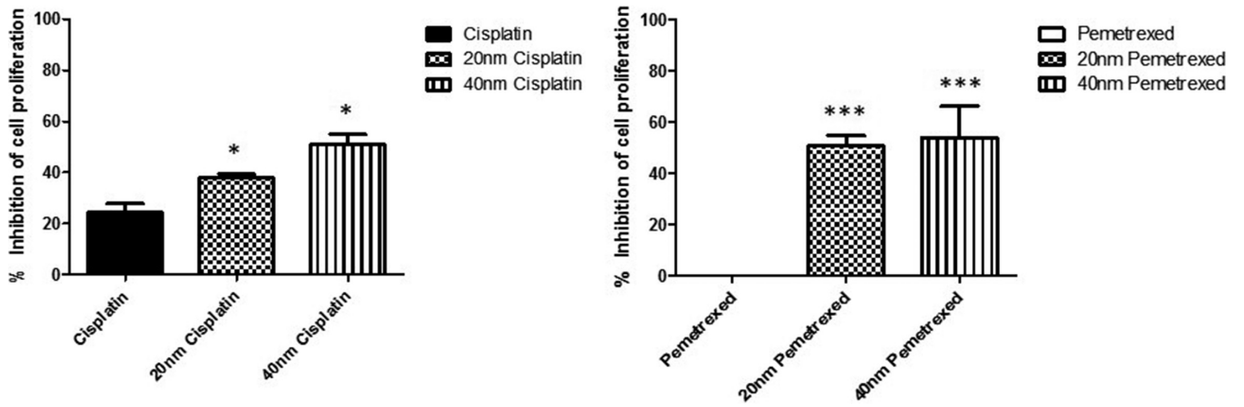

Abstract S103 Figure 1 Effect of free drug and AuNP conjugates on cancer cell proliferation. A549 cells were exposed to 10 μM cisplatin (A) or pemetrexed (B) and equimolar concentrations of 20 nm and 40 nm conjugates. Proliferation was measured at 48 hours by electrical cell-substrate impedance. Data expressed as mean ± SE (n = 3). *P < 0.05 conjugate vs free cisplatin, ***P < 0.0001 conjugate vs free pemetrexed

Conclusions We have synthesised gold-based nanomedicines that are more efficacious and biocompatible than free drug in *in vitro* cell models, suggesting these formulations could have enhanced therapeutic potency and improve patient quality of life.

S104 FACTORS AFFECTING SENSITISING EGFR MUTATION RATE AND CELL TYPE IN STAGE IIIB/IV LUNG CANCER

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Introduction Treatments for advanced lung cancer in patients with a poor performance status are limited. Such patients (PS 3–4) may not be suitable for chemotherapy for NSCLC, but may benefit from chemotherapy if SCLC is confirmed or treatment with an EGFR-TKI if an EGFR sensitising mutation (EGFR-sm) is detected. Estimates of the likelihood of detecting these two subtypes will enable patients to make informed decisions about undergoing biopsy confirmation.

Aim To analyse patient factors that affect the frequency of sensitising EGFR mutations and cell types in patients with stage IIIB/IV lung cancer.

Method Retrospective review of an electronic database of stage IIIB/IV lung cancer patients with known cell type from 2008-2013 where a quantified smoking history was available. Where EGFR testing was not performed, the estimated prevalence of EGFR-sm was extrapolated from those patients tested according to cell type. Patients with small cell and large cell lung cancer were presumed to be EGFR wild type.

Results 1033 were identified who fulfilled the inclusion criteria. Cell types were as follows: Adenocarcinoma 31.2%, Squamous Cell 23.5%, Small Cell 22.7%, NSCLC NOS 16.2% and Large Cell 6.4%.

Of 348 (33.7%) undergoing genetic testing, EGFR-sm were found in 39 (11.2%) patients. These included 32 of 241 (13.3%) adenocarcinoma, 6 of 80 (7.5%) NOS and 1 of 27 (3.7%) squamous cell. The prevalence of EGFR-sm was estimated for the 384 patients with Adenocaricinoma, NOS and Squamous Cell Carcinoma who were not tested.

Table 1 shows the effect of age and pack year smoking history on EGFR mutation status and cell type. Logistic regression analysis shows increasing pack years ($p < 0.001$) and younger age ($p = 0.004$) are associated with a lower rate of sensitising EGFR mutations. Increasing pack years is associated with a higher frequency of small cell cancers, but this is not affected by age.

Abstract S104 Table 1

		Age (years)	
		<80	80+
Smoking (pack years)	**Never**	29.1% EGFR-sm	31.8% EGFR-sm
		1.9% SCLC	10.0% SCLC
		n = 54	n = 2
	<20	8.4% EGFR-sm	15.3% EGFR-sm
		16.5% SCLC	16.7% SCLC
		n = 91	n = 3
	20+	**3.4% EGFR-sm**	5.4% EGFR-sm
		25.9% SCLC	21.4% SCLC
		n = 726	n = 112

Conclusion Smoking status significantly impacts the likelihood of detecting both EGFR-sm and SCLC, whereas age alters the likelihood of EGFR-sm alone. These data may allow a more informed discussion regarding the likelihood of detecting an actionable result in patients with advanced lung cancer with poor performance when discussing options for biopsy.

S105 MICRODROPLET DIGITAL PCR FOR THE LONGITUDINAL MONITORING OF CIRCULATING TUMOUR DNA BIOMARKERS IN UNSELECTED PATIENTS WITH ADVANCED LUNG CANCER

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Introduction and objectives Circulating cell-free tumour DNA (cfDNA) can be detected in patients with solid organ malignancies and has the potential to be used as a non-invasive biomarker. Specific mutational events can be identified in biopsies using targeted next-generation sequencing and individualised microdroplet digital PCR (mdPCR) assays designed to detect and monitor the individualised biomarker in plasma. This can inform

the timing (and sometimes mechanism) of disease progression or treatment failure.

To date this has been demonstrated in patients with EGFR and KRAS mutations.

Our objective was to determine if this approach could be applied to an unselected cohort of patients with advanced non-small cell lung cancer (adenocarcinoma subtype).

Methods Unselected treatment-naive patients with lung cancer were recruited from thoracic oncology clinics. Paired DNA from tumour biopsies and baseline/longitudinal plasma samples was obtained. Targeted next-generation sequencing (NGS) was performed using a 26-gene panel on biopsy-derived DNA. Primer sets and probes for identified mutations were optimised and validated on a the BioRad-QX100 mdPCR system.

Results The NGS data is summarised in Table 1.

Abstract S105 Table 1 Results of targeted next generation sequencing from cohort of 20 patients

Pt	Biopsy type	Total DNA loaded (ng)	Mutation 1	MAF	Mutation 2	MAF
1	Lung Biopsy	NK	EGFR exon 19 deletion	33		
2	Pleural fluid	NK	KRAS G12R	28		
3	Bronchial biopsy	33	TP53 P152S	20.42		
4	Bronchial biopsy	26	BRAF V600E	35.1		
5	EBUS	25	KRAS G12V	49.33		
6	EBUS	27	EGFR ex 19 del	63.5	TP53 R273L	36.01
7	EBUS	33	TP53 H214R	52.97		
8	EBUS	12	TP53 K132E	40.76		
9	EBUS	12	KRAS G12C	13.75		
10	EBUS	33	TP53 R283P	74.19	KRAS G12V	54.01
11	EBUS	33	KRAS G12C	39.02		
12	Lung biopsy	23	PIK3CA H1047R	28.95		
13	Lung biopsy	3	TP53 R158L	50.69		
14	Lung biopsy	4	TP53 S371Y	28.06		
15	Lung biopsy	16	TP53 1bp del/FM	24.01		
16	Lung biopsy	33	TP53 E258*	12.88		
17	Lung biopsy	33	EGFR ex 19 del	36.51		
18	Brain biopsy	33	KRAS G12L	52.46		
19	Lymph node FNA	8	No mutation	No mutation		
20	Pleural biopsy	33	TP53 C141Y	62.13		

MAF, Mutant Allele Frequency. *Both EGFR and P53 mutation detected in plasma. **Only two reports of G12L in lung cancer on COSMIC out of >20,000.

20 patients in our test cohort had stage IIIB/IV lung adenocarcinoma. These included cytology specimens – EBUS, lymph node FNA and pleural effusion, percutaneous biopsies, pleural biopsies and a brain biopsy. The mean quantity of DNA used for targeted resequencing was 23 ng. The lowest read depth for the identified mutations was 1639; in general coverage was >10,000.

19/20 patients had mutations identified in their diagnostic specimen.

12 of 20 samples had >1 mutation detected and 8 had more than 2 mutations detected at a mutant allele frequency (MAF) >10%.

CtDNA from plasma has been tested for specific mutations including in *PIK3CA*, *TP53*, and *BRAF* as well as *KRAS* and *EGFR* in these patients. In 16 of the 19 patients in which mutations were identified the mutation has also been detected in the plasma. The range of detected MAFs was between <0.1–49.6%.

It was noteworthy that there was discordance between the biomarker response and RECIST1.1 criteria in some patients.

Conclusion It is feasible to perform a targeted NGS analysis on DNA from standard fixed diagnostic lung adenocarcinoma specimens and then validate and use individualised molecular biomarkers for use in a microdroplet digital PCR assay of cell-free circulating tumour DNA. There is potential for this approach to inform clinical decision-making.

This is a robust and low cost means of monitoring treatment response non-invasively and merits further evaluation in a clinical trial.

Nintedanib or pirfenidone?

S106 CONSISTENT EFFECT OF NINTEDANIB ON DECLINE IN FVC IN PATIENTS ACROSS SUBGROUPS BASED ON HRCT DIAGNOSTIC CRITERIA: RESULTS FROM THE INPULSIS® TRIALS IN IPF

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Introduction The two replicate, randomised, placebo-controlled, 52-week INPULSIS® trials assessed the efficacy and safety of nintedanib 150 mg twice daily (bid) in patients with IPF. The primary endpoint was met in both trials; nintedanib significantly reduced the annual rate of decline in FVC compared with placebo, consistent with a slowing of disease progression.

Methods To qualify for the INPULSIS® trials if a surgical lung biopsy was unavailable, patients needed to have a high-resolution computed tomography (HRCT) scan showing honeycombing and/or a combination of reticular abnormality and traction bronchiectasis, without features suggestive of alternative causes. Surgical lung biopsies, if available, were used to confirm eligibility. A *post-hoc* subgroup analysis of patients with diagnosis based on honeycombing and/or confirmation of usual interstitial pneumonia (UIP) by biopsy versus patients with no honeycombing and no biopsy was undertaken using pooled data from both trials.

Results 723 patients (425 nintedanib, 298 placebo) had honeycombing and/or confirmation by biopsy and 338 (213 nintedanib, 125 placebo) had no honeycombing or biopsy for diagnosis of IPF. Demographics and baseline characteristics were similar between these subgroups. In patients with honeycombing and/or biopsy, the adjusted annual rate of decline in FVC was -108.7 mL/year with nintedanib and -225.7 mL/year with placebo (difference: 117.0 mL/year [95% CI: 76.3, 157.8]); in patients with no honeycombing or biopsy, it was -122.0 mL/year with nintedanib and -221.0 mL/year with placebo (difference: 98.9 mL/year [95% CI: 36.4, 161.5]). The treatment by subgroup interaction