REFERRAL RESPONSE

Sender	Recipient	F-950-003 Rev 2
iCellate Medical AB Industrivägen 1, 3rd floor 171 48 Solna Sweden +46 (0)8 789 45 45	**Demo Universitetssjukhuset** | Gastrocentrum - Stockholm 171 76 - Sweden +46 (0)800 700 00	Page 1 of 5 Reference number **ICEL00043**

BACKGROUND INFORMATION

PATIENT

First name	Last name	Gender	Age	Patient Id
Sara	Persson	female	67	19520312-0257

MEDICAL HISTORY

Cancer history	Status
Has the patient previously been diagnosed with cancer? **No**	Is the patient currently diagnosed with cancer? **Yes**
	What is the current diagnosis (diagnostic code)? **Non-small cell lung cancer**
	What is the TNM (AJCC staging system) and tumor burden (by CT or MRI)? **TNM 2A, tumor burden 4 cm (diameter)**
	Past, current and planned treatment cycles? **Neoadjuvant Cisplatin chemotherapy. Radiotherapy. Surgical exploration and anatomic resection. Lymph node sampling. Targeted therapies?**

Family
Have any of the patient's parents, siblings or children been diagnosed with cancer? **NA**

SAMPLING

Date & Time for sampling	Referring physician	Additional information
16/06/2019 09:00	Dr Erna Test Vali	A 67-year-old lady presents with shortness of breath and coughing up of blood-stained mucus. Never-smoker. Chest X-ray computed tomography (CT) shows pulmonary nodules. Clinical stage II. Tissue sample provides pathologic confirmation of non-small cell lung cancer, favouring subtype adenocarcinoma. ECOG performance status 0 (Fully active, able to carry on all pre-disease performance without restriction). Tissue samples are insufficient for molecular analysis. A follow up tissue based analysis is planned if no oncogenic driver is found. No contact with relatives, family history therefore unknown. Question: EGFR mutations? BRAF V600E mutations? ALK gene rearrangements? ROS1 rearrangements? NTRK gene fusions? KRAS mutations?

Service ordered	Number of tubes	Total blood volume	Courier	Tracking number
# 20011: **gDNA** **ctDNA** PANEL	5	35 ml	Fast Courier	218739101-98

Received at iCellate	Report issued	Sample satisfactory/macroscopic inspection	Analysis type	Comment
06/17/2019 11:00am	06/20/2019 11:45am	yes	Clinical	

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RESULTS

SEQUENCING (NGS) PERFORMED BY

Illumina sequencing provider

ctDNA

Oncogenic variants

GENE	VARIANT	ZYGOSITY	POTENTIAL TREATMENT MODALITY*	LEVEL OF EVIDENCE**	ALLELE FREQUENCY	REFERENCE
EGFR	L858R	N/A	Gefitinib	1	0,1%	Douillard JY, Ostoros G, et al. First-line gefitinib in Caucasian EGFR mutation-positive NSCLC...
EGFR	L858R	N/A	Erlotinib	1	0,1%	Rosell R, Carcereny E, Gervais R, et al. Erlotinib versus standard chemotherapy as first line...
EGFR	L858R	N/A	Afatinib	1	0,1%	Yang JC, Wu YL, Schuler M, et al. Afatinib versus cisplatin based chemotherapy for EGFR mutation...

Organ of origin
(If not already known)

ORGAN NAME	VALUE
Lung	Diagnosed

METHOD DESCRIPTION

**Please note that the literature survey is not a treatment suggestion from iCellate Medical AB. The treating physician must decide if the suggestions are relevant for the patient.*

*** doi: 10.1200/PO.17.00011. Standard Therapeutic Implications - 1 FDA-recognized, 2 Standard care, 3 Compelling clinical evidence, 4 Compelling biological evidence, Standard Resistance Implications - R1Standard care, R2 Compelling clinical evidence.*

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gDNA (inherited risk factor evaluation)

Oncogenic variants						
GENE	VARIANT	ZYGOSITY	POTENTIAL TREATMENT MODALITY*	LEVEL OF EVIDENCE**	ALLELE FREQUENCY	REFERENCE
None						

Organ at risk	
ORGAN NAME	VALUE

METHOD DESCRIPTION

**Please note that the literature survey is not a treatment suggestion from iCellate Medical AB. The treating physician must decide if the suggestions are relevant for the patient.*

*** doi: 10.1200/PO.17.00011. Standard Therapeutic Implications - 1 FDA-recognized, 2 Standard care, 3 Compelling clinical evidence, 4 Compelling biological evidence, Standard Resistance Implications - R1Standard care, R2 Compelling clinical evidence.*

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CONCLUSION

PATIENT HISTORY

A 67-year-old lady with shortness of breath and coughing up of blood-stained mucus, diagnosed with non-small cell lung cancer of histologic type adenocarcinoma. Clinical stage T2a with tumor 4 cm in greatest dimension without apparent lymph node involvement. Cytotoxic treatment started prior to
molecular testing. The treatment effect on cell viability has not been determined, and neither tumor viability nor cell proliferation is known. The patient is fully active, able to carry on all pre-disease performance without restriction. Tissue samples were insufficient for molecular analysis. A follow up tissue based analysis is planned if no oncogenic driver is found. No contact with relatives. Family history and therefore any genetic predisposition for cancer not known.

GENETIC TESTING DIGEST

An EGFR activating variant was detected, but no BRAF V600E, KRAS, ERBB2, RET or MET mutations, ALK gene rearrangements, ROS1 rearrangements, or NTRK gene fusions.

The most common mutations in the EGFR gene are deletions in exon 19 in 45% of patients with EGFR mutations and a point mutation in exon 21 (L858R) in 40%. Both mutations result in activation of the tyrosine kinase domain, and both are associated with sensitivity to the small molecule EGFR tyrosine kinase inhibitors (TKI), including erlotinib, gefitinib, afatinib, osimertinib and dacomitinib. Patients without activating mutations in EGFR should not be treated with TKI.

The following somatic EGFR mutation was detected: L858R, based on the blood plasma sample when compared to the germline sample. No tissue biopsy was made available for testing. No oncogenic germ line variants were detected. This variant results in activation of the tyrosine kinase domain of EGFR, a potential part of the disease mechanism. It is also associated with sensitivity to the tyrosine kinase inhibitors erlotinib, gefitinib, afatinib, osimertinib and dacomitinib. The predictive effect of the discovered variant is well defined and the patient has a significantly better response.

No germline or somatic EGFR T790M variant was detected. This variant is one of those which is associated with a lack of responsiveness to EGFR tyrosine kinase inhibitor therapy (i.e. resistance). It is also associated with familial (inherited) lung cancer predisposition and would have warranted genetic counselling if detected in the germline.

Erlotinib or gefitinib is recommended as first line therapy by clinical guidelines. Afatinib is also recommended as first line therapy based on decreased cough, dyspnea and improved health-related quality of life compared to those receiving cisplatin/pemetrexed, although Afatinib was potentially associated with 4 treatment-related deaths. Progression free survival is improved with systemic therapy with these tyrosine kinase inhibitors compared to cytotoxic systemic therapy, although overall survival is not different. Erlotinib has fewer treatment-related severe side effects and deaths than does cytotoxic therapy.

Most patient’s tumors become resistant, i.e. the disease progresses, within 9.7 to 13 months. If the disease progresses it is recommended to perform additional testing at that point to establish the potential cause and a therapy, if available.

AUTHORIZED BY

REPORT AUTHORIZE BY
Christer Ericsson
Chief Scientific Officer
iCellate Medical AB

CLINICAL AUTHORIZATION
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