MULTICENTER EVALUATION OF THE IDYLLA™ GENEFUSION CARTRIDGE IN LUNG CANCER

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Introduction

- Incidence of lung cancer worldwide is high and most patients have a poor prognosis with a **5-year survival** rate in metastatic disease of only **5%**
- All patients with metastatic NSCLC **should be tested before the first line of therapy** for pathogenic driver mutations in *EGFR, BRAF, ERBB2, MET$_{ex14}$* and fusions in *ALK, ROS1, RET* and *NTRK1/2/3* genes
- As the available material is often scarce, **multiplex technique** is the best approach, like that developed by biocartis **(Idylla™ GeneFusion assay)**

Idylla™ GeneFusion Assay

- Detection of **ALK, ROS1, RET, NTRK1/2/3 fusions & METex14 skipping mutations**
- Currently available in Research Use Only
- Fully automated test **directly from FFPE tissue** without the need for RNA extraction
- Turnaround time: **3 hours**
- 2 detection technology types:
  - **Specific fusion detection (spe)** of the most relevant gene fusions by RT-qPCR
  - **Expression imbalance (imb)** by analyzing expression ratios 5'- 3'

Material and Methods

- Multicenter study (18 centers)
- **313 FFPE tissue samples** from lung cancer patients with molecular data previously obtained by reference methods (FISH, RT-PCR +/- NGS) : **97 ALK, 44 ROS1, 20 RET, 3 NTRK1, 2 NTRK3, 32 *MET$_{ex14}$*** and **115 WT samples**
- 1-3 sections of 5µm FFPE with ≥ 10% tum cell content
- 3 types of results : detected, not detected and invalid
- Definition of inconclusive cases : i) if more than one fusion or METex14 skipping mutation are detected; ii) if the invalid gene is the one that has been detected as altered by the ref method

Overall results

- Valid results : 306/313 cases (98%)
- Idylla™ confirmed the alteration in 165/193 (85%) and absence of alteration in 107/113 (95%) negative samples
- Idylla™ failed to detect 23 fusions and 5 METex14

Idylla™ vs reference method	ALK	ROS1	RET	MET	NTRK
positive percentage agreement	94% 82/87	95% 36/38	100% 17/17	100% 27/27	100% 3/3
negative percentage agreement	93% 193/205	97% 255/263	99% 289/290	98% 275/280	99% 288/290
Overall concordance	94%	97%	99%	99%	99%

Aim of this study : to compare the results of Idylla™ GeneFusion prototype with those obtained by reference methods (FISH, RT-PCR and NGS)

Results (Gene per gene)

ALK

Idylla™ \ Routine reference methods	Alteration	No alteration	Total
Alteration	82	**5**	87
No alteration	**12**	193	205
Invalid	3	18	21
Total	97	216	**313**

Sensitivity	85%
Specificity	98%
Pos % agreement	94%
Neg % agreement	93%

RET

Idylla™ \ Routine reference methods	Alteration	No alteration	Total
Alteration	17	**0**	17
No alteration	**1**	289	290
Invalid	2	4	6
Total	20	293	**313**

Sensitivity	85%
Specificity	100%
Pos % agreement	100%
Neg % agreement	99%

METex14

Idylla™ \ Routine reference methods	Alteration	No alteration	Total
Alteration	27	**0**	27
No alteration	**5**	275	280
Invalid	0	6	6
Total	32	281	**313**

Sensitivity	84%
Specificity	100%
Pos % agreement	100%
Neg % agreement	98%

ROS1

Idylla™ \ Routine reference methods	Alteration	No alteration	Total
Alteration	36	**2**	38
No alteration	**8**	255	263
Invalid	0	12	12
Total	44	269	**313**

Sensitivity	82%
Specificity	99%
Pos % agreement	95%
Neg % agreement	97%

NTRK

Idylla™ \ Routine reference methods	Alteration	No alteration	Total
Alteration	3	**0**	3
No alteration	**2**	288	290
Invalid	0	20	20
Total	5	308	**313**

Sensitivity	60%
Specificity	100%
Pos % agreement	100%
Neg % agreement	99%

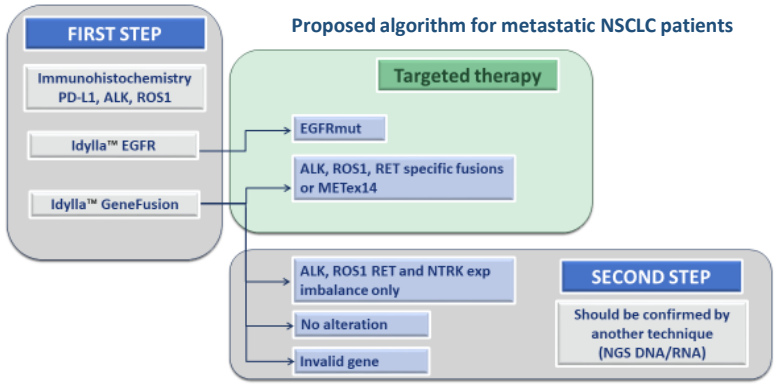
- **Negative samples** : 107/113 cases
  - ✓ 6 false positive cases (5 ALKimb and 1 ROS1 spe/imb)
  - ✓ 2 inconclusive cases (2 alterations found by Idylla)
- **Inconclusive samples** : N=7

6 cases (2 alterations found by Idylla) :
- ✓ 1 (ALKimb/spe + MET) and 1 (ALKimb/spe + NTRK) : ALK confirmed
- ✓ 2 (ALKimb + RETimb/spe) : RET confirmed
- ✓ 1 (ALKimb + ROS1imb) and 1 (ALKimb + MET) : negative

1 ALK positive found ALKimb invalid with no ALK specific detection

Conclusion

- Idylla™ allows in **3 hours** the detection of ALK, ROS1, RET, NTRK fusions and METex14 with a **good concordance**
- All of the ALK, ROS1 and RET **specific fusion detection** identified by Idylla™ were confirmed by ref method, except for 1 ROS1
- **ALK and ROS1 imbalance only should be confirmed** (8 false positive samples)
- Idylla™ GeneFusion : good method to offer, along with Idylla™ EGFR testing in metastatic NSCLC patients, **who cannot wait for treatment**



Confilcts of interest : *Biocartis (congress fees) ; AstraZeneca, Roche, Pfiser, MSD (Board and scientific collaborations)*

This eposter will be presented at the symposium on Monday, August 30th (11:45-13:15)