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3MO - Comprehensive biomarkers (BMs) analysis to predict efficacy of PD1/L1 immune checkpoint inhibitors (ICIs) in combination with chemotherapy: a subgroup analysis of the Precision Immuno-Oncology for advanced Non-Small CELL Lung CancER (PIONeeR) trial

Fabrice Barlesi, Laurent Greillier, Florence Monville, C Audigier-Valette, S. Martinez, N. Cloarec, Sylvie van Hulst, L. Odier, Frédéric Vely, L. Juquel, et al.

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ESMO IMMUNO-ONCOLOGY

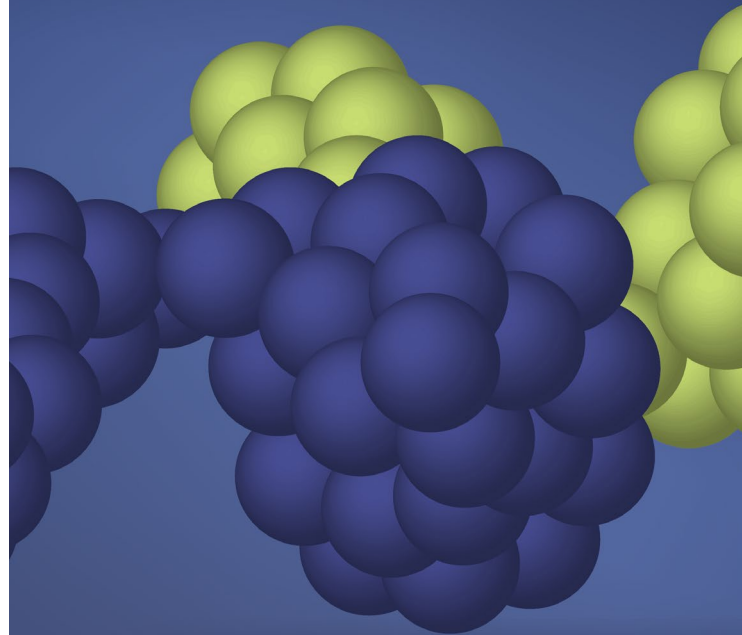
Annual Congress

COMPREHENSIVE BIOMARKERS ANALYSIS TO PREDICT EFFICACY OF PD1/L1 ICI IN COMBINATION WITH CHEMOTHERAPY

A subgroup analysis of the Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (PIONeR) trial

F. Barlesi^{1,2}, L. Greillier^{4,5}, F. Monville⁶, C. Audigier Valette⁷, S. Martinez⁸, N. Cloarec⁹, S. Van Hulst¹⁰, L. Odier¹¹, F. Vely^{3,5}, L. Juquel^{3,5}, L. Arnaud⁵, S. Bokobza¹², M. Hamimed⁴, M. Karlsen¹³, P. Dufosse¹³, A. Pouchin⁵, L. Ghezali⁶, M. Le Ray⁵, J. Fieschi-Meric⁶, S. Benzekry¹³

1- Gustave Roussy, Villejuif, France 2- Université Paris Saclay, Faculté de Médecine, Kremlin Bicêtre, France 3- Aix Marseille Université, Marseille, France 4- CRCM - Inserm U1068, CNRS UMR7258, Aix Marseille Université, Institut Paoli-Calmettes, Marseille, France 5- Assistance Publique-Hôpitaux de Marseille (APHM), Marseille, France 6- Veracyte SAS, Marseille, France 7- Centre Hospitalier Sainte-Musse, Toulon, France 8- Centre Hospitalier d'Aix-en-Provence, Aix-en-Provence, France 9- Centre Hospitalier Henri Duffaut, Avignon, France 10- Centre Hospitalier de Nîmes, Nîmes, France 11- Hôpital Nord-Ouest, Villefranche-sur-Saône, France 12- Innate Pharma, Marseille, France 13- Inria, Nice - Sophia Antipolis, France



DECLARATION OF INTERESTS

Fabrice Barlesi, MD, PhD

Personal financial interests:

- None (since August 2021)

Institutional financial interests:

- Abbvie, ACEA, Amgen, Astra-Zeneca, Bayer, Bristol-Myers Squibb, Boehringer–Ingelheim, Eisai, Eli Lilly Oncology, F. Hoffmann–La Roche Ltd, Genentech, Ipsen, Ignyta, Innate Pharma, Loxo, Novartis, Medimmune, Merck, MSD, Pierre Fabre, Pfizer, Sanofi-Aventis and Takeda

Non-financial interests:

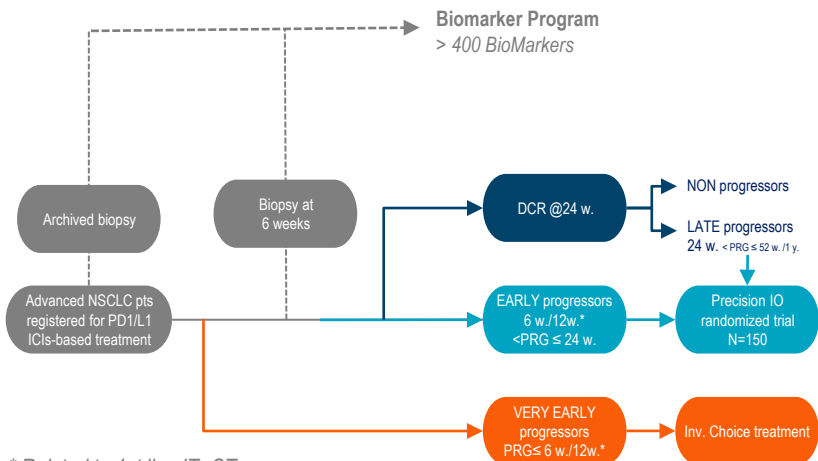
- Principal Investigator for Astra-Zeneca, BMS, Innate Pharma, Merck, Pierre Fabre and F. Hoffmann-La Roche, Ltd, sponsored trials (or ISR)

No other conflicts of interest

THE PIONEER STUDY DESIGN

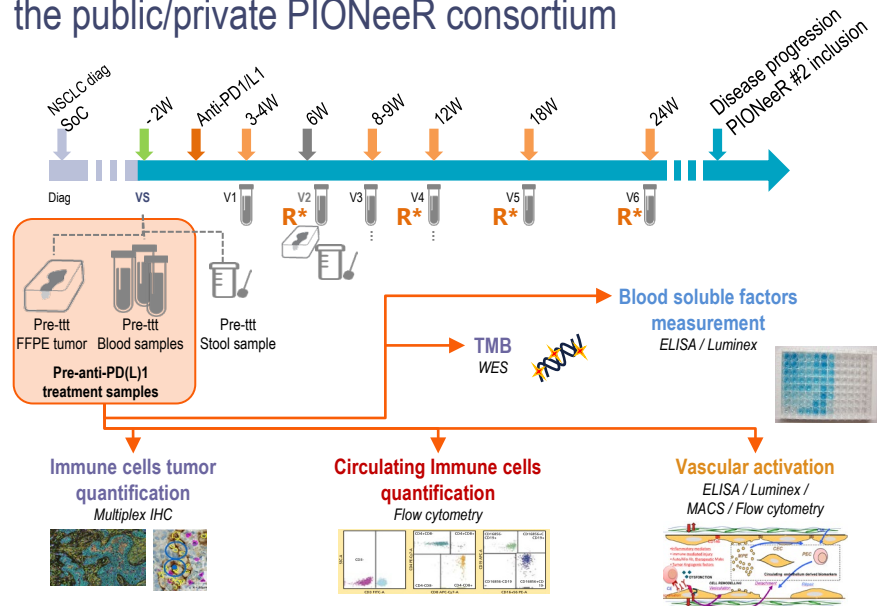
Assess, Understand & Overcome ICI resistances in advanced NSCLC

Baseline, On-treatment & Progression biopsies
Both 2nd and 1st line settings



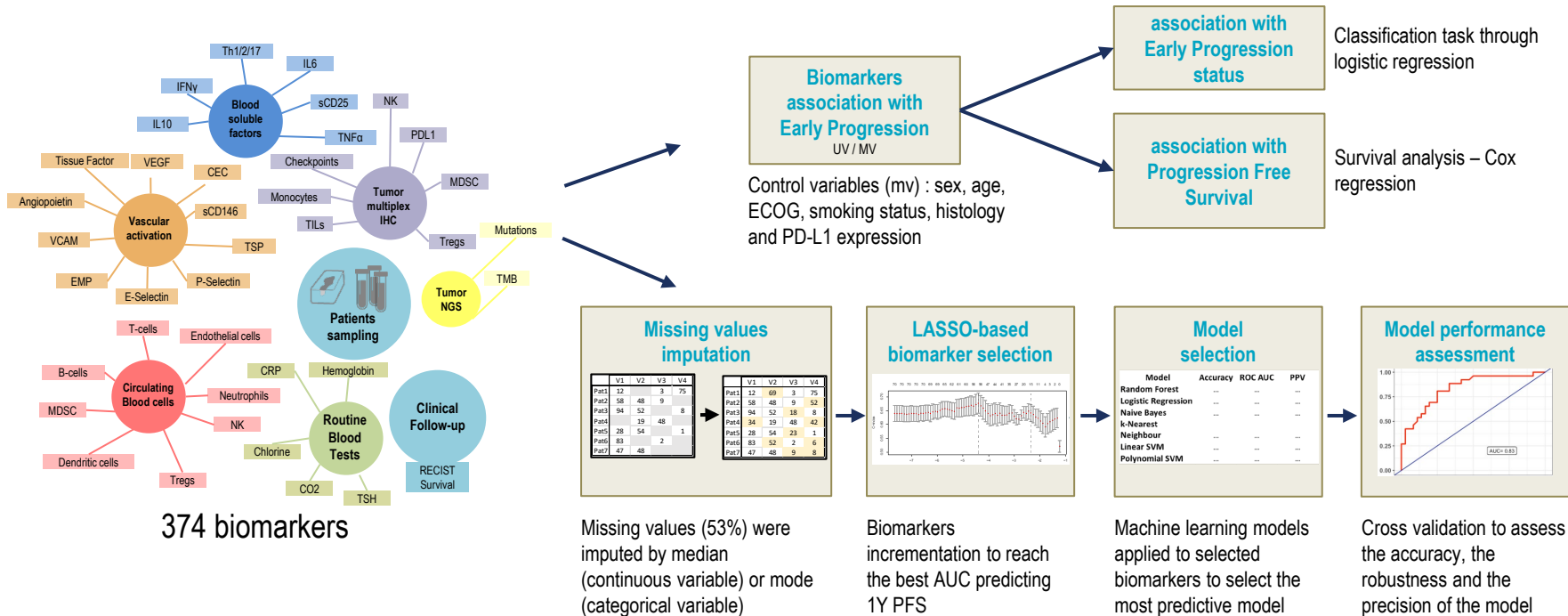
* Related to 1st line IT+CT

A comprehensive biomarkers assessment, thanks to the public/private PIONeer consortium



GENERATE A MULTIMODAL PREDICTIVE SIGNATURE

Aim: predict patients deriving the largest long-lasting PFS benefit



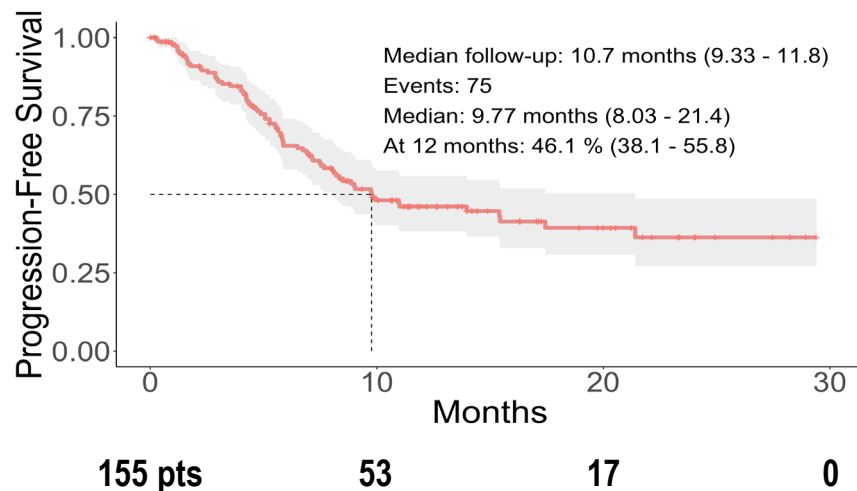
PATIENTS CHARACTERISTICS & OUTCOMES

Overall, 350 pts included to date - Focus on the 1st line setting*

To date, 155 pts treated with Chemo/Pembrolizumab

PFS outcomes in line with reported results

SEX	M	101 (65%)	PD-L1 EXPRESSION	≥1%	43 (35%)
	F	54 (35%)		<1%	81 (65%)
AGE	<70	127 (82%)	BIOPSY SITE	Not interpretable	31
	≥70	28 (18%)		Metastasis	51 (38%)
ECOG	0	68 (44%)	HISTOLOGY	Primitive tumor	85 (62%)
	1	86 (56%)		Unknown	19
	Unknown	1		ADK	98 (84%)
TOBACCO HISTORY	Current	55 (37%)	TREATMENT	Others	4 (3.4%)
	Never	7 (4.7%)		Squamous	15 (13%)
	Previous	88 (59%)		Unknown	38
RECIST	Unknown	5	RECIST	anti-PD1	6 (3.9%)
				anti-PDL1	0 (0%)
				PEMBRO+CHEMO	149 (96%)
				CR	8 (7.1%)
				PD	4 (3.5%)
		PR	60 (53%)		
		SD	41 (36%)		
		Unknown	42		



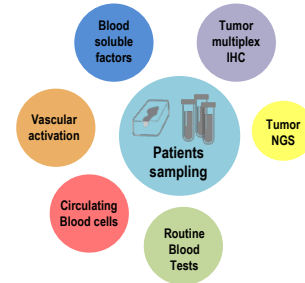
RESULTS: STANDARD ANALYSIS

Biomarkers associated with PFS (1st line setting only)

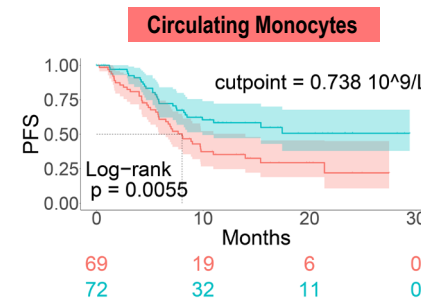
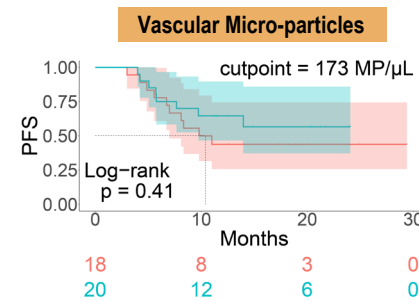
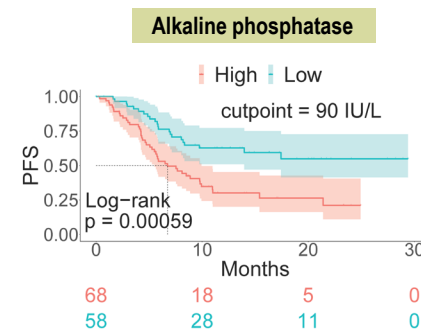
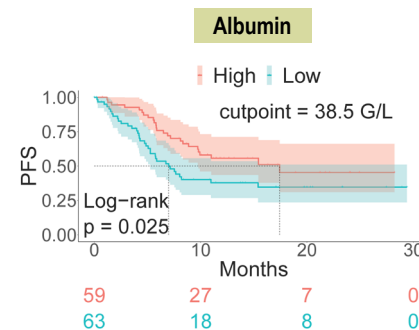
Global Table (Univariate/Multivariate Analyses)

Variable	UV		MV	
	HR	p	HR	p
Albumin	0.71 (0.55 - 0.92)	**	0.47 (0.31 - 0.7)	***
Alkaline phosphatase	1.5 (1.3 - 1.8)	****	1.4 (1.2 - 1.7)	***
C reactive protein	1.6 (1.3 - 2.1)	***	1.9 (1.3 - 2.7)	***
Chlorine	0.66 (0.51 - 0.85)	**	0.6 (0.43 - 0.82)	**
Circulating Monocytes	1.4 (1.1 - 1.7)	*	1.6 (1.2 - 2.2)	**
VEGFR1	1.4 (1 - 2.1)	*	1.9 (1.2 - 2.8)	**
Platelets	1.3 (1 - 1.6)	*	1.5 (1.2 - 2)	**
ASAT	1.3 (1 - 1.6)	*	1.7 (1.2 - 2.5)	**
PD-L1 ≥ 1%	2.2 (1.2 - 3.8)	**	2.7 (1.3 - 5.7)	**
Prothrombin rate	0.65 (0.49 - 0.87)	**	0.55 (0.35 - 0.87)	*
Total bilirubin	1.5 (1.2 - 1.9)	***	1.6 (1.1 - 2.3)	*
Circulating Neutrophils	1.3 (1 - 1.6)	*	1.4 (1.1 - 2)	*
Vascular Micro-particles	1.6 (1.1 - 2.2)	**	1.7 (1.1 - 2.7)	*
Circulating Leukocytes	1.4 (1.1 - 1.7)	**	1.5 (1 - 2.1)	*
Stromal Monocytic MDSC	0.55 (0.31 - 0.98)	*	0.27 (0.081 - 0.92)	*

UV= univariable, MV= multivariable, ****= p<0.0001, ***= p<0.001, **= p<0.01, *= p<0.05

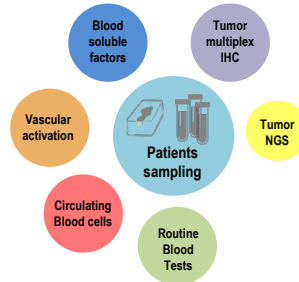


Selected PFS curves

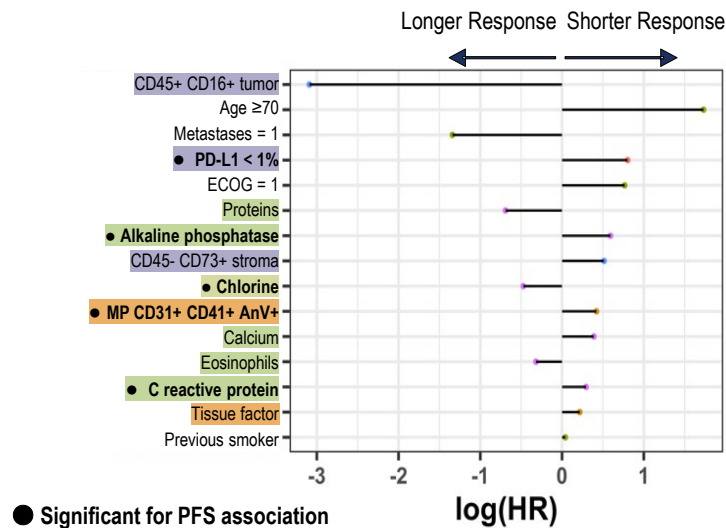


RESULTS: MACHINE LEARNING

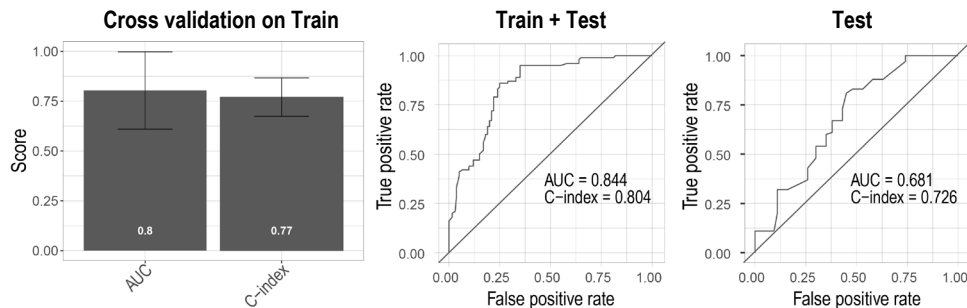
Biomarkers associated with PFS (1st line setting only)



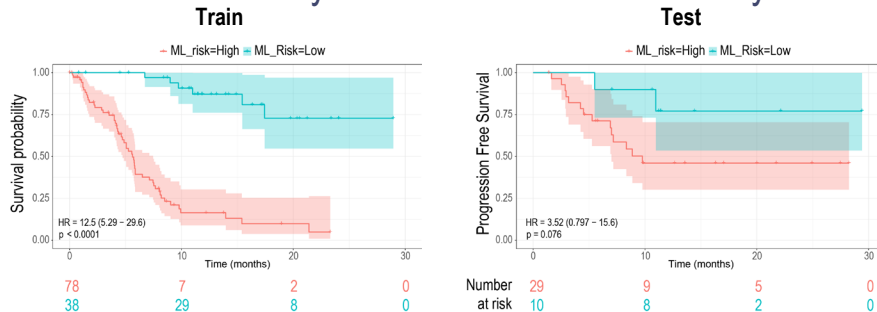
A 15-biomarkers signature



Training set (n=116, 75%), Testing set (n=39, 25%)



Prediction of the 1-year PFS with 83% sensitivity



CONCLUSIONS

A multimodal signature predicts the 1st line chemo/ICI benefit in advanced NSCLC pts

- Our 15-biomarkers signature includes clinical, biological, tissue and circulating biomarkers
- Our predictive algorithm achieves good c-index and AUC in both cross-validation and testing set cohorts
- Variability of the cross-validation results is due to multiple samples still remaining to be processed; the completion of the study is expected in 2023
- The predictive model will be dissected at the pathophysiological level and an external validation will be performed on other cohorts

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Patients & Families

Investigators and Study teams

Marseille (& area)

- APMH Mult. Oncology & Therap Innov. Dep. : Pr L. Greillier, Dr P Tomasin
- St Joseph Private Hospital : Dr. C. Foa
- Europ. Hospital : Dr. J. Le Treut
- Ste Musse CHI, Toulon : Dr. C. Audigier-Valette
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- Bastia Hospital : Dr. P. Bory
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- Nîmes Hospital : Dr. S. Van Hulst
- Avignon Hospital : Dr. N. Cloarec

Lyon (& area)

- Léon Bérard Center Medical Oncology Department : Dr. M. Pérol
- Villefranche Hospital : Drs. L. Falchero, L. Odier
- Annecy Hospital : Dr. S. Hominal

Toulouse (& area)

- Toulouse CHU Thoracic Oncology Department : Pr. J. Mazières
- Cahors Hospital : Dr. P. Barre
- Montauban Hospital : Dr. S. Zahi
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- VasculoMonitoring Platform : Pr. F. Sabatier, L. Arnaud
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- J. Fieschi, F. Monville, L. Ghezali & team

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- D. Olive & teams

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- Methodologists: Dr. D. Pérol, S. Chabaud, C. Cropet

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European Society for Medical Oncology (ESMO)

Via Ginevra 4, CH-6900 Lugano

T. +41 (0)91 973 19 00

esmo@esmo.org

esmo.org

