1404P Safety of nintedanib plus docetaxel in advanced non-squamous NSCLC (nsNSCLC) patients: The preliminary results of the SENECA (second-line nintedanib in non-small cell lung cancer) trial

A.M. Morelli[1], M.R. Migliorino[2], A. Morabito[3], R. Chiari[4], F. Grossi[5], P. Bordi[6], F. Di Costanzo[7], A. Delmonte[8], G. Romano[9], A. Misino[10], V. Scotti[11], V. Gregorc[12], S. Pisconti[13], G.L. Ceresoli[14], A. Del Conte[15], I. Colantonio[16], L. Ciuffreda[17], E. Capelletto[1], I. Stura[18], S. Novello[1]

[1]Department of Oncology, University of Turin, AOU San Luigi, Orbassano, Italy, [2]UOSD Pneumologia Oncologica, Azienda Ospedaliera San Camillo Forlanini, Rome, Italy, [3]Thoracic Medical Oncology, Istituto Nazionale Tumori, "Fondazione G. Pascale" - IRCCS, Naples, Italy, [4]Medical Oncology, Santa Maria della Misericordia Hospital, Perugia, Italy, [5]Lung Cancer Unit, Ospedale Policlinico San Martino, Genoa, Italy, [6]Medical Oncology Unit, University Hospital, Parma, Italy, [7]Medical Oncology, AOU Careggi, Florence, Italy, [8]Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) - IRCCS, Meldola, Italy, [9]UO Oncologia, Ospedale Vito Fazzi, Lecce, Italy, [10]Oncology Unit, Clinical Cancer Center "Giovanni Paolo II", Bari, Italy, [11]Radiation Oncology Unit, Oncology Department, Azienda Ospedaliero-Universitaria Careggi, Florence Italy, [12]Department of Oncology, IRCCS Ospedale San Raffaele, Milan, Italy, [13]S.C. Oncologia Medica, P.O.C.SS. Annunziata - S.G. Moscati, ASL Taranto, Statte, Italy, [14]Medical Oncology, Humanitas Gavazzeni, Bergamo, Italy, [15]Oncology Unit, Centro di Riferimento Oncologico (CRO) - IRCCS, Pordenone, Italy, [16]Medical Oncology, St. Croce e Carle General Hospital, Cuneo, Italy, [17]S.C. Oncologia Medica I, A.O.U. Città della Salute e della Scienza di Torino, Presidio Molinette, Turin, Italy, [18]Department of Public Health and Paedriatic Sciences, University of Turin, Turin, Italy

Background: The SENECA trial, a phase IIb, open label, multicentre study, aimed to investigate in the real life efficacy and safety of nintedanib plus docetaxel, used weekly (T1) or q3wks (T2), in pretreated nsNSCLC patients, stratified for relapse-timing (within or over 3 months from end of first-line therapy). Preliminary efficacy data have been previously presented: no difference in median Progression Free-Survival and a similar trend in Overall Survival between T1 and T2 were showed. Weekly docetaxel has better tolerability than q3wks administration: aim of this study is to evaluate two different docetaxel schedules combined with nintedanib, in order to potentially maximize their use.

Methods: Baseline characteristics have been already presented. Incidence and severity of treatment-related Adverse Events (AEs) were evaluated from beginning of treatment until 28 days after its completion, according to Common Terminology Criteria for Adverse Events (CTCAE) version 3, in 167 patients (receiving at least one dose of study drugs) enrolled in 18 Italian oncologic centres, between January 2016 and March 2018.

Results: Incidence of any grades AEs was numerically higher in T2 compared to T1 (484 vs 450 events, respectively); a complete overview of AEs ($\geq$ 5% incidence in either group) is reassumed in Table1. Docetaxel was reduced in 14.4% patients, more frequently in T2 vs T1 (18.8% vs 9.7%). Nintedanib reduction was needed in 19.8% of patients, 23.2% in T1 and 15.3% in T2, mainly for diarrhea. Thirty-one (18.6%) patients permanently discontinued study drugs (11 in T1 vs 20 in T2) due to hypersensitivity reactions and pain.

Table: 1404P Main AEs observed in the SENECA trial according to docetaxel schedule and CTCAE grade

	N = 167					
AEs	T1 (N = 82)	T2 (N = 85)	p-value	T1 (N = 82)	T2 (N = 85)	p-value
	Any Grades			Grade $\geq$ 3		
Fatigue	44(53.6%)	56(65.9%)	0.10	5(6.1%)	10(11.7%)	0.20
Diarrhea	41(50%)	40(47%)	0.70	4(4.8%)	4(4.7%)	0.95
ALT elevation	24(29.3%)	17(20%)	0.16	4(4.8%)	5(5.9%)	0.77
Afebrile Neutropenia	11(13.4%)	45(52.9%)	<0.0001	3(3.6%)	17(20%)	<0.0001
Pain	19(23.2%)	21(24.7%)	0.81	3(3.6%)	2(2.3%)	0.62
Anemia	18(21.9%)	16(18.8%)	0.61	1(1.2%)	1(1.2%)	0.30
Nausea	17(20.7%)	14(16.5%)	0.47	3(3.6%)	3(3.5%)	0.96
Dyspnea	16(19.5%)	18(21.2%)	0.78	2(2.4%)	2(2.3%)	0.97
Fever	15(18.3%)	9(10.6%)	0.15	2(2.4%)	0(0%)	0.14
Cough	13(15.8%)	14(16.5%)	0.91	0(0%)	0(0%)	NE
Decreased Platelets	11(13.4%)	2(2.3%)	0.007	0(0%)	0(0%)	NE
Skin Toxicity	11(13.4%)	9(10.6%)	0.57	0(0%)	1(1.2%)	0.32
Oral Mucositis	10(12.2%)	19(22.3%)	0.08	3(3.6%)	1(1.2%)	0.29
GGT elevation	9(11%)	10(11.8%)	0.87	3(3.6%)	5(5.9%)	0.50
Vomiting	7(8.5%)	15(17.6%)	0.08	0(0%)	1(1.2%)	0.32
Decreased leukocytes	5(6.1%)	10(11.8%)	0.20	0(0%)	2(2.3%)	0.16
AST elevation	6(7.3%)	6(7%)	0.94	2(2.4%)	1(1.2%)	0.53
Dysgeusia	6(7.3%)	5(5.9%)	0.70	0(0%)	0(0%)	NE
Parestesie	4(4.9%)	1(1.2%)	0.38	7(8.5%)	0(0%)	0.97

ALT: alanine aminotrasferase; NE: not evaluable; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase.

Conclusions: Preliminary safety data of SENECA trial show statistically significant differences only in a few of the items explored (particularly afebrile neutropenia), but underline a clear trend of higher tolerability for weekly docetaxel combination treatment in second line nsNSCLC patients.

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