

MIM Toscana 2015/2016

- **Focolaio epidemico di NM ST11, gruppo C**
- Area: Firenze, Prato, Empoli
- **61 casi (2013-14: solo 5 casi)**
- 11 casi in soggetti stranieri
- **13 casi in vaccinati** (7 casi da > 5 anni o < di 1 mese)
- **Letalità generale 13 (21%)**
- Letalità nei vaccinati 1/13 (8%)
- Letalità non vaccinati 12/48 (25%)
- **Sequela permanente: 7 (perdita udito, amputazioni)**

IMD, serogroup C: Tuscany 2015-2016

Pts characteristics	All patients	Meningitis	Meningitis + Meningococccemia	Meningococccemia
	56	4	25	27
Mean age (range)	35 (1-83)	28 (20-37)	37 (8-75)	32 (1-83)
Clonal complex 11 (43)	41	2	21	18
<i>Purpura fulminans</i>	16 (29%)	0	4 (16%)	12 (44%)
Septic shock	32 (57%)	2 (50%)	13 (52%)	17 (63%)
In-hospital mortality	13 (23%)	0	2 (8%)	11 (41%)

Patients characteristics

Pts characteristics	All patients	Meningitis	Meningitis + Meningococemia	Meningococemia
	56	4	25	27
Vaccinated	13 (23%)	1 (25%)	5 (20%)	7 (26%)
> 5 years	5	0	2	3
< 1 month	2	0	1	1
Steroid therapy (51)	38 (74%)	4	17 (68%)	17 (63%)
Intensive care (53)	40 (75%)	4	20 (80%)	16 (59%)
LOS, mean days (range)	17.5	14 (12-15)	11 (1-36)	20 (1-111)
Sequelae (43)	7 (17%)	1	3	3
In-hospital mortality	13 (23%)	0	2 (8%)	11 (41%)

Patients characteristics according to the outcome

Characteristics:	Deaths (13 cases)	Survivors (43 cases)	p.
Male sex	6 (46%)	21 (49%)	1
Mean age	44 (1-83)	31,4 (3-70)	
Clinical presentation:			
Meningitis (4)	0	4 (9%)	0,598
Meningitis + Meningococccemia (25)	2 (15%)	23 (53%)	0.007
Meningococccemia (27)	11 (85%)	16 (37%)	0.035
<i>Purpura fulminans</i> (16)	9 (69%)	7 (16%)	<0.001
Septic shock (32)	13 (100%)	19 (44%)	0.001
Vaccination (13)	1/12 (8%)	12/41 (29%)	0.271
Selected bio-chemisty parameter			
WBC count mmc (mean)	7.112	17.433	
PLT count mmc (mean)	79.666	151.654	
PCT ng (mean)	122,3	36	
Time from onset to ED (days)	0,8	1,6	
Need for ICU (40)	9 (69%)	31 (72%)	1
Steroid therapy (38)	6 (46%)	32 (74%)	0.116

Sequence type (ST) & clonal complex (CC)

TABLE 1. Serogroups of representative clonal complexes

Country	ST11 complex/ ET37 complex	ST213	ST22	ST23 cluster/ lineage A3	ST269	ST32	ST41/44 complex/ lineage 3	ST5 subgroup 3	ST 4821
A	0	0	0	0	0	0	0.1	97.3	1.9
B	7.9	72.9	6.8	2.3	76.5	84.7	76.3	0.3	50.6
C	61.6	2.1	1.3	0.8	4.2	3.0	4.3	0.8	28.1
W	19.6	0.2	54.3	2.1	0.2	0.1	0.1	0	3.1
X	0	0	0.3	0	0	0.1	0.2	0.1	1.3
Y	0.6	0	7.6	69.9	0.1	0.2	0.3	0.1	0
NG	0.6	6.4	17.2	9.0	3.4	2.6	5.7	0.7	0.6
Others	9.7	18.4	12.5	17.9	15.6	9.3	13.0	0.5	14.4

ST, sequence type.
Numbers are the percentages of isolates of *Neisseria meningitidis* from representative clonal complexes that express the serogroup shown. Data are from the Neisseria MLST website (<http://pubmlst.org/neisseria/>).

STUDIO SUI PORTATORI SANI DI MENINGOCOCCO ARS TOSCANA

Indagine di prevalenza

Soggetti di età 11-45 anni che si recano per qualunque vaccinazione negli ambulatori

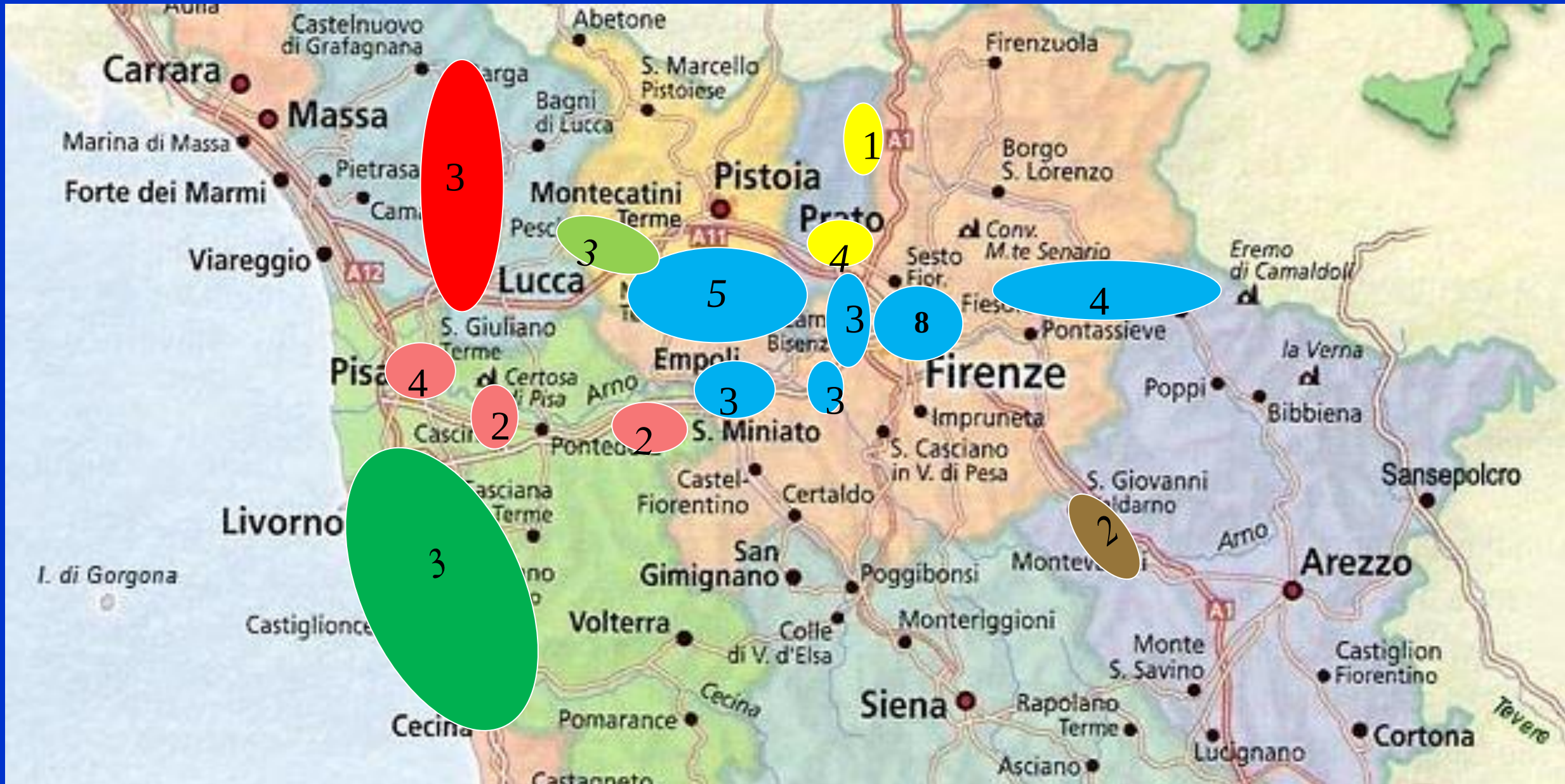
AREA DI STUDIO: USL Toscana Centro (ex Asl 10 di Firenze, ex Asl 11 di Empoli);

AREA DI CONTROLLO: USL Toscana Sud-Est (ex Asl 7 di Siena, ex Asl 9 di Grosseto).

Eseguiti 2.287 tamponi, circa 600 per ogni ex asl (300 nella fascia 11-19 anni, 300 nella fascia 20-44 anni).

Durata dello studio: 1 marzo 2016 – 1 giugno 2016

Sierogruppo C: Distribuzione per Aree e Province 2015-16



STUDIO SUI PORTATORI SANI DI MENINGOCOCCO

Tamponi positivi per sierogruppo, metodo di analisi ed ex asl

Sierogruppo	Metodo colturale					PCR				
	FI	EMP	SI	GR	Tot	FI	EMP	SI	GR	Tot
A	0	0	0	0	0	0	0	0	0	0
B	6	9	5	4	24	10	10	11	6	37
C	0	0	0	0	0	0	3	0	1	4
W	0	0	0	0	0	0	0	0	0	0
Y	0	3	4	2	9	0	4	4	3	11
Z	0	1	0	0	1	0	1	0	0	1
29E	1	1	0	0	2	1	1	0	1	3
Non tipizzati	27	16	9	18	70	1	1	0	0	2
Totale positivi	34	30	18	24	106	12	20	15	11	58
Tamponi analizzati	597	595	494	601	2.287	597	595	494	601	2.287
Rapporto percentuale	5,7	5,0	3,6	4,0	4,6	2,0	3,4	3,0	1,8	2,5

Potential role of IgM-enriched Immunoglobulin as adjuvant treatment for Invasive Meningococcal Disease

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- We retrospectively reviewed 111 cases of IMD documented in Italy, in Tuscany region (53 cases) and Naples metropolitan area (58 cases), from October 2013 to December 2016.
- All were treated with standard antibiotic and supportive therapy and either with (35 patients) or without (76 patients) IgM-enriched Immunoglobulin.
- We analysed the impact of adjuvant treatment together with several variables, including demographics, type of IMD, serogroup of *Neisseria meningitidis* and management, on mortality or permanent sequelae..

Results:

- Death or permanent sequelae were documented in 9% (3/35) of patients treated with IgM-enriched Ig as compared to 30% (23/76) of patients not receiving adjuvant therapy, a statistically significant difference (p 0.023).
- The multivariate regression analysis confirmed adjuvant therapy as the only independent factor protecting patients with IMD from death or permanent sequelae (OR 0.202, 95% CI 0.046-0.909, p 0.036).
- Factors associated with a higher risk of death or permanent sequelae were increased age (OR 1.029, 95% CI OR 1.003-1.005, p 0.030) and *purpura fulminans* (OR 8.869, 95% CI OR.733-28.775, p <0.001).

Table 1: Comparison between patients receiving or not IgM-enriched Ig therapy

Variables	IgM-enriched Ig therapy YES (n = 35)	IgM-enriched Ig therapy NO (n = 76)	P
Age [years]	21 [3 - 31]	29 [18 - 50]	0.033
Males	23 (66%)	40 (53%)	0.277
Tuscany region patients	9 (26%)	44 (58%)	0.003
<i>N. meningitidis</i>, serogroup C	11 (31%)	46 (61%)	0.008
SOFA score [range]	4 [2 - 7]	4 [2 - 7]	0.680
Clinical manifestations of IMD:			
· Meningitis	1 (3%)	19 (25%)	0.011
· Meningococccemia	11 (31.4%)	26 (34%)	0.942
· Meningitis + Meningococccemia	23 (66%)	30 (39%)	0.018
· <i>Purpura fulminans</i>	7 (20%)	16 (21%)	1.000
· Severe coagulopathy (DIC)	13 (37%)	23 (30%)	0.616
· Septic shock	12 (34%)	41 (54%)	0.085
Empirical therapy with Ceftriaxone	30 (86%)	67 (88%)	0.958
Use of steroid therapy	32 (91%)	59 (79%)	0.168
Days from clinical onset to empirical therapy	1 [1 - 2]	1 [1 - 2]	0.497
Death or Permanent disease	3 (9%)	23 (30%)	0.023

Table 2. Factors influencing death or permanent sequelae (univariate & multivariate analysis).

Variables	Univariate analysis		Multivariate analysis	
	OR [95% CI]	p	OR [95% CI]	p
IgM-enriched Ig	0.216 [0.060 – 0.777]	0.019	0.202 [0.046 – 0.909]	0.036
Age	1.023 [1.004 – 1.043]	0.020	1.029 [1.003 – 1.005]	0.030
<i>Purpura fulminans</i>	8.752 [3.234 – 22.715]	<0.001	8.869 [2.733 – 28.775]	<0.001
Severe Coagulopathy (DIC)	4.057 [1.676 – 9.821]	0.002		
Septic Shock	4.714 [1.814 – 12.249]	0.001		
SOFA score	1.219 [1.094 – 1.358]	<0.001		
Tuscany region	3.176 [1.302 – 7.746]	0.011	-----	-----
Serogroup C	4.064 [1.575 – 10.487]	0.004	-----	-----

Conclusions:

In our retrospective analysis, IgM-enriched Immunoglobulin adjuvant therapy seems to favourably impact on mortality or permanent sequelae in patients with IMD. Prospective, randomized clinical trials are therefore warranted