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## Precise reply and clarifications on behalf of Sicilian Public Health Authorities to the case report published by La Rosa and colleagues

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### ABSTRACT

As a results of the case report “Post-rotavirus vaccine intussusception in identical twins: a case report” recently published on Human Vaccines & Immunotherapy by La Rosa et al., the principal Sicilian Public Health Authorities decided to specify several points and underline some important details omitted by the authors. In particular, aims to underline the remarkable benefit for Sicilian Regional Health service after the introduction of the rotavirus vaccination.

Universal mass vaccination against rotavirus is properly managed by the Regional Health Authorities and is contributing to a consistent increase of public health in the Sicilian pediatric population; any modification of such a program should be based on robust scientific evidences. Finally, a single case report should not be considered as a basis to recommend a change in the clinical practice but instead a possible point of start for discussion and research.

### ARTICLE HISTORY

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### KEYWORDS

Immunization schedule; intussusception; pediatric population; rotavirus vaccination

Dear Sirs,

We read with interest the paper by La Rosa et al “Post-rotavirus vaccine intussusception in identical twins: a case report” recently published on Human Vaccines & Immunotherapy.<sup>1</sup>

In our opinion, some points need to be specified, in particular to underline the remarkable benefit for Sicilian Regional Health service after the introduction of the universal mass vaccination against rotavirus (UMRV), that was omitted by the authors.<sup>1</sup>

G.G. and Y are two identical twins, born in Province of Catania, the 16th of June 2013. The twins were born at a gestational age of 36 + 0 weeks, that was internationally recognized as a preterm birth, and not an “at term” birth how reported.<sup>1,2</sup>

Weight (in grams), length and cranial circumference (in centimeters) at birth were 2,150 - 31 - 46 (for X), and 2,050 - 31.5 - 46 (for Y) respectively. The 3rd of September 2013 the pediatrician correctly recommended, according to the Regional Immunization Schedule approved in 2012 and become law the 1st of January 2013, the oral administration of monovalent rotavirus vaccine (RV1) for both twins.<sup>3</sup>

We agree with the Authors that universal mass vaccination against rotavirus (UMVR) exerts a large public health impact on rotavirus burden of disease. Sicily was the first region in Italy to introduce UMVR in 2012. After the first year, a 40% reduction of rotavirus gastroenteritis hospitalization among children aged 0-59 months was recorded, in spite of suboptimal

vaccination coverage, consistently with figures observed in other European Countries.<sup>4-9</sup>

Nevertheless, in the paper by La Rosa et al there are some statements that, in our opinion, deserve further discussion as summarized below:

- 1) The use of monovalent rotavirus vaccine (RV1) is approved for preterm babies and such a vaccination is internationally recommended.<sup>10,11</sup> Intussusception insurgence was probably related with several factors (viral or bacterial infections, feeding, familiar predisposition, use of drugs, ...) and was reported only a marginal role of the new generation of rotavirus vaccine.<sup>12-15</sup> However, the preterm condition might act as a confounding factor to the occurrence of intussusception in the twins.
- 2) Being the twins been born in June 2013, the vaccine was administered in September 2013 and not in 2014 as reported.<sup>1</sup> RV1 vaccination after 24 weeks of age would have constitute an off label administration, as specified in the Summary of the Product Characteristics (SmPC).<sup>10</sup>
- 3) In Sicily, all the public health providers, including pediatricians, are trained and requested to follow the Regional Immunization Schedule, verifying the absence of vaccine contraindication in babies and children and counseling the families for a consciousness adherence to vaccination programs.<sup>4,7</sup> Thus, the sentence reported in the paper by La Rosa et al. (“...on the advice of the pediatrician..”) should be interpreted in this light.

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- 4) Health care providers and pediatricians in Sicily properly report any intussusception case. Such an attitude reflected in an increasing trend of intussusception hospitalizations among children aged 0-59 months in the pre-rotavirus vaccination period, due to contributing factors different from RV vaccination (2003-2012).<sup>14,16</sup> Twins were hospitalized for intussusception 7 and 8 d after vaccine first dose administration, respectively. Such a time frame is in line with the findings of different post marketing surveillance studies and the monovalent vaccine SmPC.<sup>10,15, 17</sup> In fact, an increase of 1.6 intussusception cases out of 100.000 vaccinations was recently postulated on the basis of the VAERS monitoring in the USA after nearly 11 million of doses of RV1 distributed.<sup>18</sup> For the time being, the rate of RV1 temporarily associated intussusceptions in Sicily is in line with such an estimate.
- 5) In January 2016, started a case control study that will investigate all invagination cases hospitalized in Sicily from 2009 to 2014, comparing socio-demographics, neonatal, feeding, familiar, pharmacological and genetic factors (through an oral swab), with control children comparable for gender, gestational age and environmental characteristics. Familiarity of intussusceptions hypothesized by authors, is an intriguing theory. However the interview of the twins' mother and family pediatrician, recently carried out during the study, reduced the link with an intussusception familiarity. As a matter of fact, any twins relative, including parents and the 2 older brothers had never experienced any episode of intussusceptions. The statements made by La Rosa et al in the paper on this potential association lack of scientific evidence (and references) and thus should be framed as an authors personal opinions.
- 6) Finally, during the interview, emerged the use of drugs for both twins in the 2 d preceding the hospitalization for intussusception. In particular, from the 9th of September 2013, due to a urinary tract infection, was administered to X an antibiotic (Cefpodoxime) and, from the same day, due to a bronchospasm with associated cough, were administered to Y a nebulized solution of salbutamol and ipratropium bromide. This possible confounding factor was supported by several studies that analyzed the possible role in particular of antibiotics in intussusception insurgence.<sup>19-21</sup>

In conclusion, in agreement with the Evidence Based Medicine concept, we believe that a single case report should not be considered as a basis to recommend a modification in the clinical practice but instead a possible point of start for scientifically sound discussion and research, if needed. UMVR is properly managed by the Regional Health Authorities and is contributing to a consistent increase of public health in the Sicilian population; any modification of such a program should be based on robust scientific evidences.

#### Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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