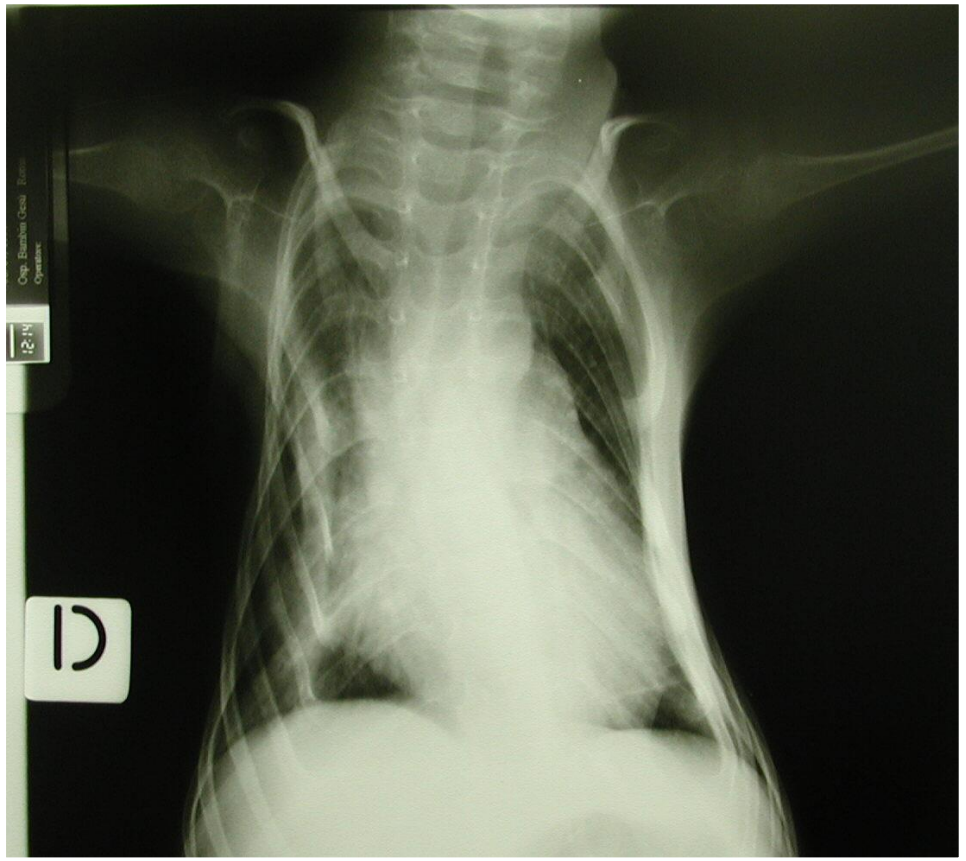
SMA type 1

- Female
- 3 months, weigth 4.5 kg, heigth 51 cm
- In last month failure to thrive
- Feeding diffuculties
- Suspected swallowing abnormalities

- **Paradoxycal breathing**
- **Global hypotonia, no head/neck control**
- **No deep tendon reflexes**
- **Tongue fasciculations**

- **SpO_2 96 % in Room Air; HR 150 bpm; RR 25 b/m**



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Neuromuscular Disorders 25 (2015) 979–989

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Workshop report

1st Italian SMA Family Association Consensus Meeting: Management and recommendations for respiratory involvement in spinal muscular atrophy (SMA) types I–III, Rome, Italy, 30–31 January 2015

V.A. Sansone [1,*,a], F. Racca [2,a], G. Ottonello [3], A. Vianello [4], A. Berardinelli [5], G. Crescimanno [6], J.L. Casiraghi [7] on behalf of the Italian SMA Family Association

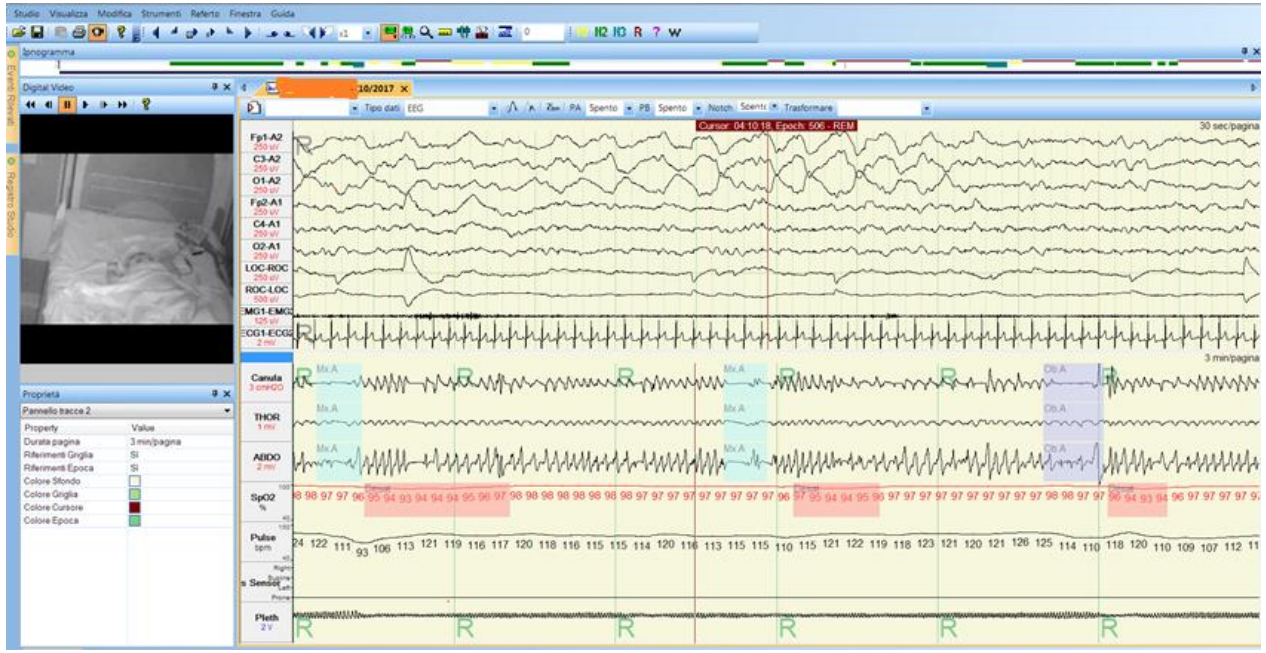
Table 2
Summary of recent criteria for sub-classification in the different SMA types, with reference to prognosis and relation to SMN2 copy numbers.

SMA type	Age at onset	Maximum function achieved	Sub-classification	Prognosis	SMN2 copy number
0 (very severe)	Neonatal, prenatal signs	Never sits	–	If untreated: death by 1st month	
1 (severe)	0–6 months	Never sits, some never achieve head control	1a: onset in neonatal period, head control never achieved 1b: onset after neonatal period, usually by 3 months; head control never achieved 1c: onset usually after 3 months, head control achieved	If untreated death by 2 years, better response to treatment if onset after 3 months	1 or 2 SMN2 copies in most (80%) pts
2 (intermediate)	7–18 months	Sits, not stands	According to functional level, decimal classification ranging from 2.1 to 2.9	Survival into adulthood; possible respiratory problems	3 SMN2 copies in >80% pts
3 (mild)	>18 months	Stands and walks	3A: onset before 3 years; 3B: onset after 3 years	Survival into adulthood, walking can be lost in patients with earlier onset	3 or 4 SMN2 copies
4 (adult)	10–30 years	Stands and walks	–	Survival into adulthood, usually walking preserved	4 or more SMN2 copies

How do you assess gas exchanges at the first referral?

1. ABG analysis
2. Pulse - oximetry + blood gases analysis
3. Pulse - oximetry + $tcPCO_2$ monitoring
4. Pulse - oximetry + $etPCO_2$ monitoring
5. Full PSG/Poligraphy + $tcPCO_2$ monitoring

Full PSG + tcPCO2 monitoring- SMA 1



Total sleep time h	7.23
Sleep Efficiency (TST/T in bed)	82.4
REM %	29.7
N1%	1.6
N2%	49.9
N3%	18.5
Mean SaO2 (%)	96
Minimal SaO2 (%)	91
SaO2 <90% (%TST)	0,0
ODI (n.desat >4%/h)	2.1
AHI (n° /h)	12.5
Central Apnea Index	0,1
Periodic Breathing (% time)	9
mean tcCO2 (mmHg)	46
maximal tcCO2 (mmHg)	52
Time >50 mmHg(%TST)	11

ABG pH 7,47; pO_2 65.5 mmHg; pCO_2 32.2 mmHg ; SaO_2 96.8%; EB – 0.8 mEq/l

Given the results what would you do?

Total sleep time h	7.23
Sleep Efficiency (TST/T in bed)	82.4
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1. Wait and see
2. Start CPAP
3. Start NIV
4. Supply oxygen
5. Other

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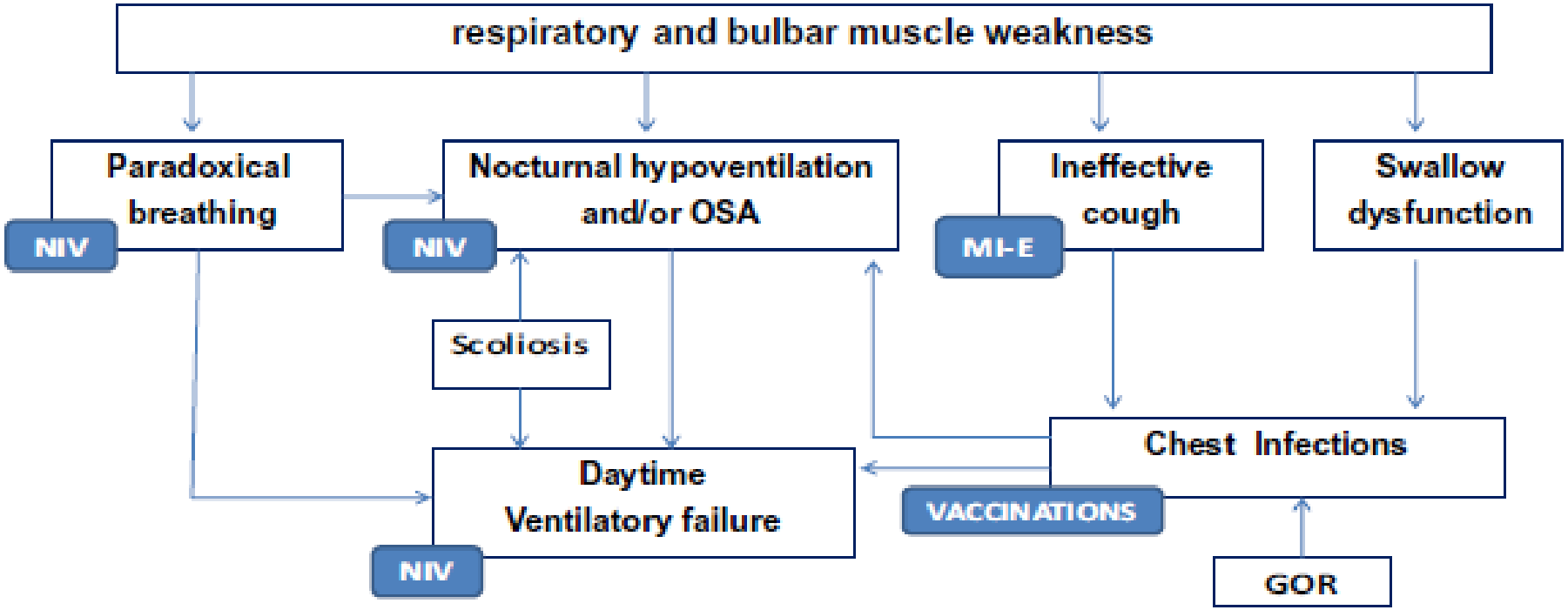

Fig. 1. Summary of pulmonary problems and respiratory interventions in spinal muscular atrophy.

Special Issue Article

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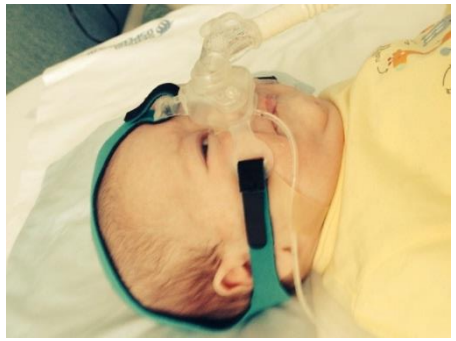
Consensus Statement for Standard of Care in Spinal Muscular Atrophy

Ching H. Wang, MD, PhD, Richard S. Finkel, MD, Enrico S. Bertini, MD, Mary Schroth, MD, Anita Simonds, MD, Brenda Wong, MD, Annie Aloysius, MRCSLT, HPC, Leslie Morrison, MD, Marion Main, MCSP, MA, Thomas O. Crawford, MD, Anthony Trela, BS, and Participants of the International Conference on SMA Standard of Care

- NIV with bilevel positive pressure support has been studied most frequently, although there is no evidence to suggest any 1 type of ventilator interface is superior
- In addition, the optimal settings for NIV have not been established
- In general, NIV settings are individualized to achieve adequate inspiratory chest wall expansion and air entry and normalization of oxygen saturation and end-tidal carbon dioxide or transcutaneous CO_2 measurements
- NIVshould be combined with airway clearance techniques

WHAT WOULD YOU DO?

- Which ventilation mode? (PSV S/T, AVAPS, ACV)
- Which interface? (nasal, oro-nasal, full face masks)
- O_2 supplementation?



Training NIV- SMA 1

Ventilation mode: PSV ST + Vtg

EPAP [cmH2O]	4
IPAP max [cmH2O]	17
Vtg [ml]	50
Rise time	1
Trigger INSP	1
RR [b/m]	24
T insp min [sec]	0.8

Bambino Gesù
OSPEDALE PEDIATRICO

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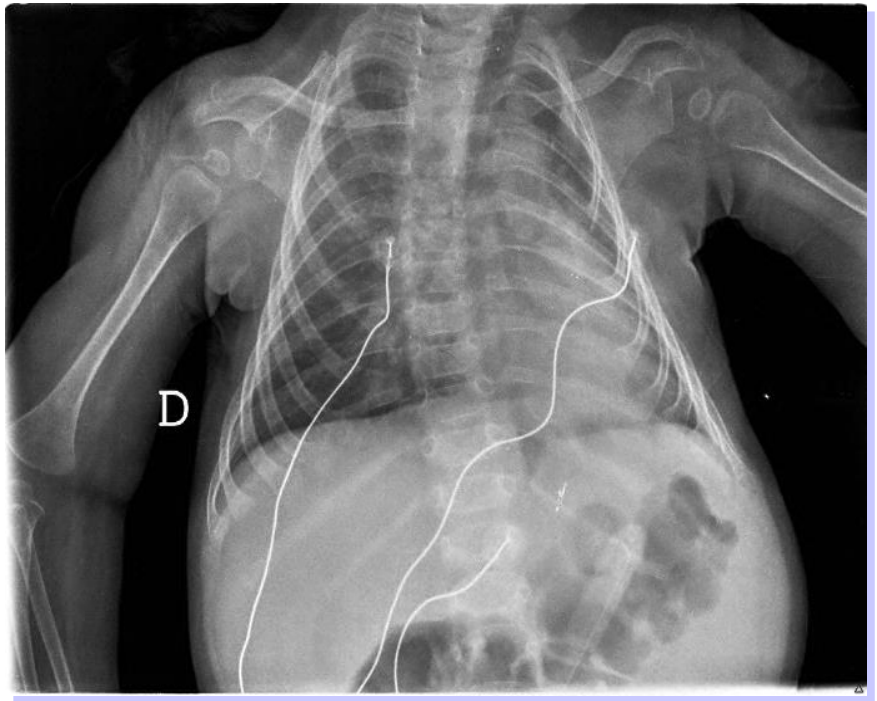
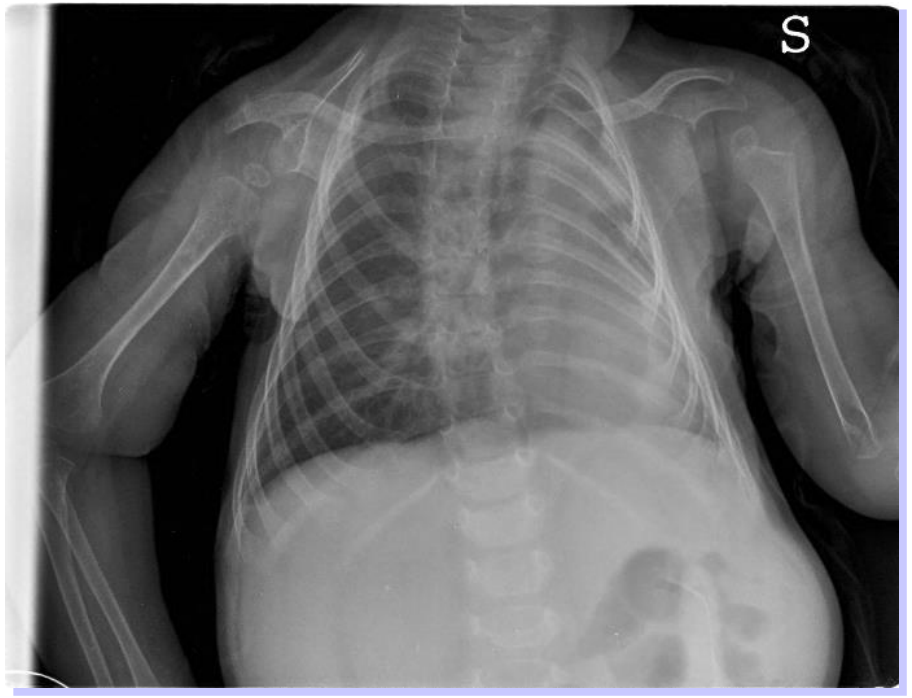
OSPEDALE PEDIATRICO

Complications

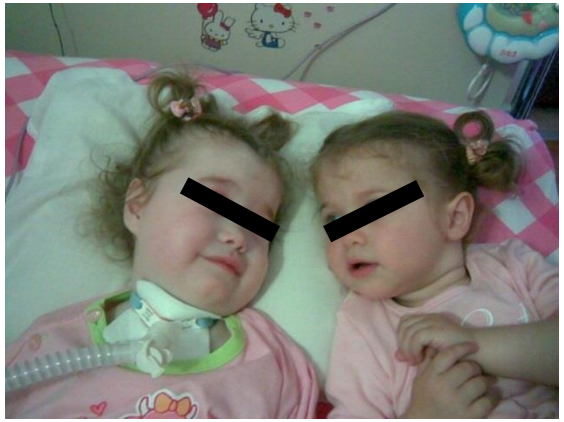
- Desaturations, **SpO2 80%, HR 150 bpm, FR 50 b/m**
- Increased respiratory secretions
- ABG pH 7.28 pCO2 64 mmHg



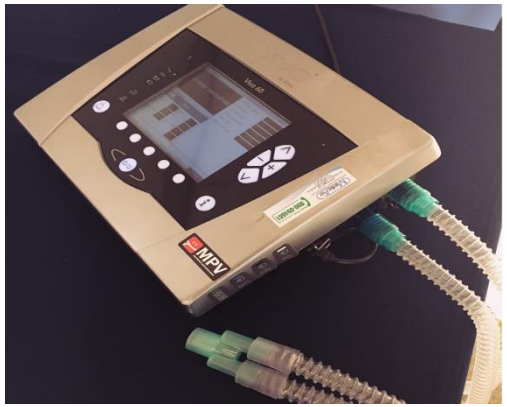


Management of Acute Respiratory Failure

- Intensive chest physioterapy and cough – machine assist
- Severe desaturations wich needed manual respiratory assistance
- OTI
- Failed 3 extubation attempts
- tracheostomy + VMI
- PEG
- Switch to home ventilator



Invasive mechanical ventilation



Ventilation mode: PSV ST + Vtg

EPAP [cmH2O]	5
IPAP max [cmH2O]	17
Vtg [ml]	50
Raising time	1
Trigger INSP	1
RR [b/m]	22
T insp min [sec]	0.9

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Controindications to NIV and indication to IMV

Table 2 Contraindications to non-invasive and indication to invasive ventilation

Contraindications to non-invasive ventilation
Swallowing disorders
History of pulmonary aspiration secondary to gastroesophageal reflux and or vocal cord paralysis
Inability to tolerate non-invasive ventilation
Indication of invasive pressure ventilation
Failure to adequately ventilate with non-invasive ventilation
Failure to tolerate non-invasive ventilation
High level of dependence on assisted ventilation (16–20 h/day)

Tracheostomy and home ventilation in children

Raouf S. Amin[a*], Cynthia M. Fitton[b]

Seminars in Neonatology (2003) 8, 127–135

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Controindications to NIV and indication to IMV

- Deterioration in patient's condition
- Failure to improve or deterioration in arterial blood gas tensions
- Development of new symptoms or complications such as pneumothorax, sputum retention, nasal bridge erosion
- Intolerance or failure of coordination with the ventilator
- Failure to alleviate symptoms
- Deteriorating conscious level
- Patient and carer wish to withdraw treatment

BTS GUIDELINE

Non-invasive ventilation in acute respiratory failure

British Thoracic Society Standards of Care Committee

Thorax 2002;57:192–211

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How do you assess IMV?

1. ABG analysis
2. Pulse - oximetry + blood gases analysis
3. Pulse - oximetry + $tcPCO_2$ monitoring
4. Pulse - oximetry + $etPCO_2$ monitoring
5. Full PSG/Poligraphy + $tcPCO_2$ monitoring

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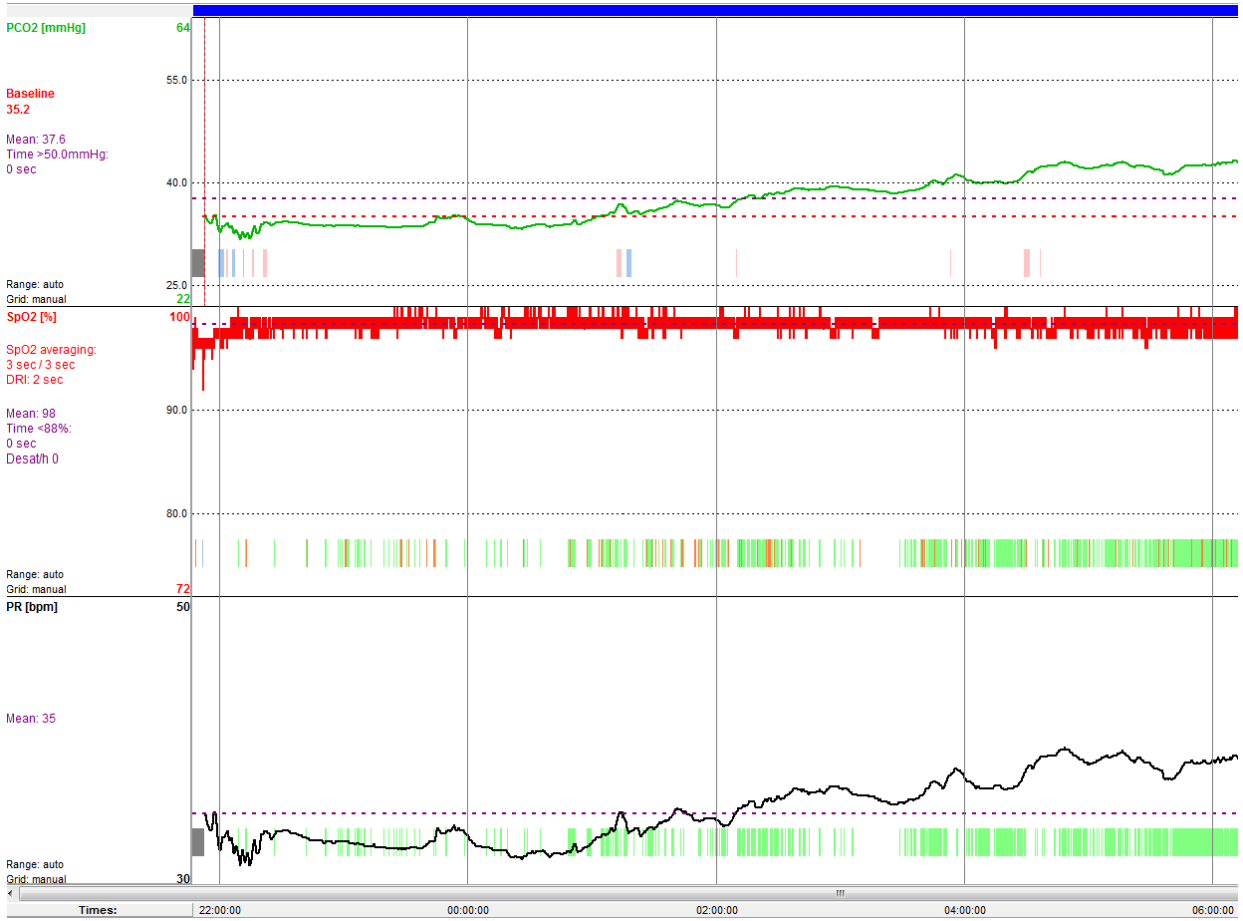
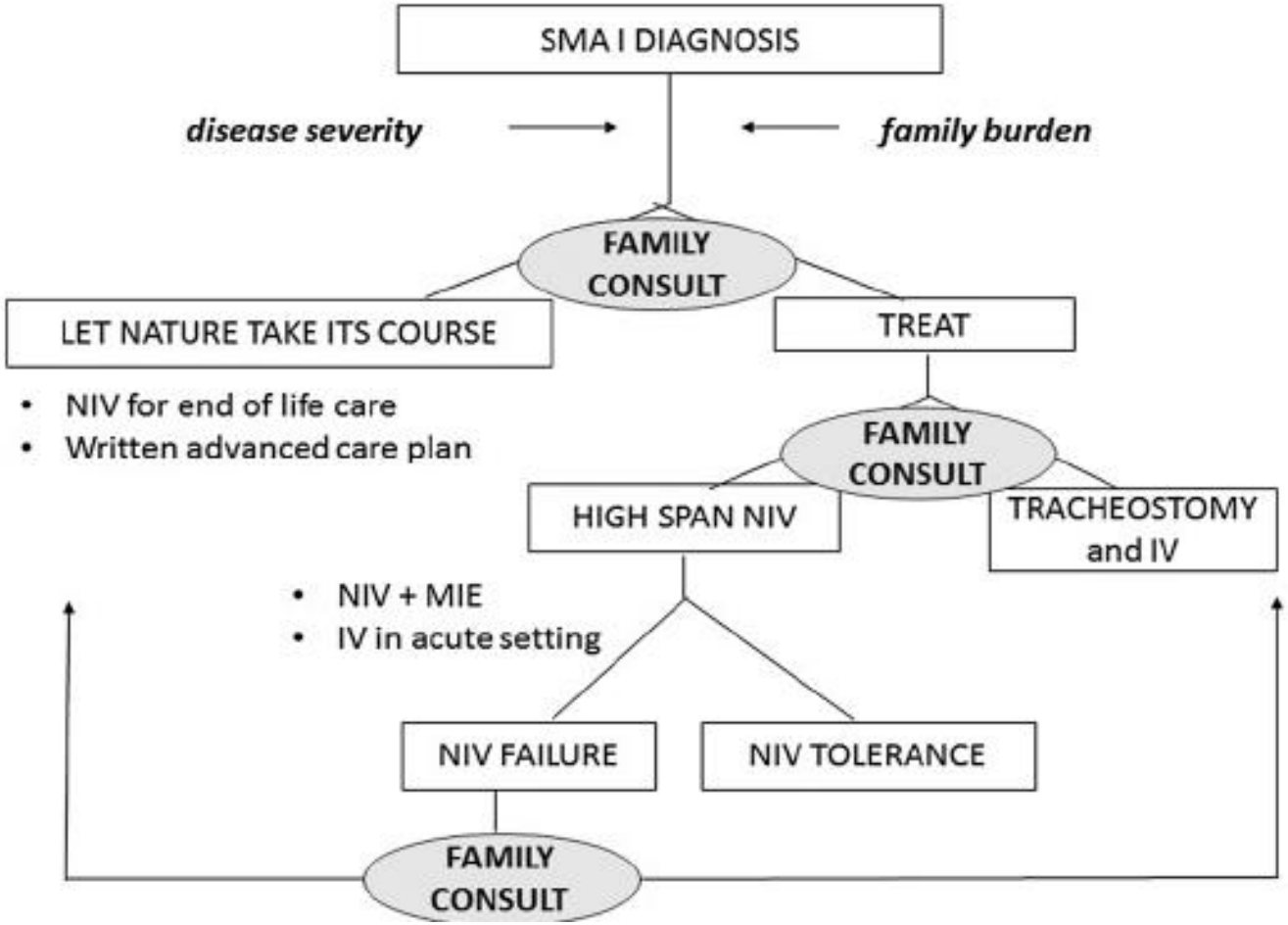
Pulse - oximetry + $TcPCO_2$ monitoring IMV



Mean SaO2 (%)	97
Minimal SaO2 (%)	92
SaO2 <90% (%TST)	0,0
ODI (n° desat >4%/h)	0,0
mean tcCO2 (mmHg)	37.6
maximal tcCO2 (mmHg)	43,3
Time >50 mmHg(%TST)	0,0

1st Italian SMA Family Association Consensus Meeting: Management and recommendations for respiratory involvement in spinal muscular atrophy (SMA) types I–III, Rome, Italy, 30–31 January 2015



There is evidence that anticipatory respiratory management including airway clearance with assisted cough, non invasive or invasive ventilatory support and adequate nutritional care are associated with longer survival in SMA1. However, there is still debate on the choice of long term ventilation in patients affected by SMA1.

Sansone et al. /Neuromuscular Disorders 25 (2015) 979–989

PAEDIATRIC RESPIRATORY REVIEWS (2008) 9, 45–50

Paediatric Respiratory Reviews

CME ARTICLE

The use of mechanical ventilation is appropriate in children with genetically proven spinal muscular atrophy type I: the motion for

John R. Bach*

Department of Physical Medicine and Rehabilitation, UMDNJ-New Jersey Medical School, Newark, NJ, USA

PAEDIATRIC RESPIRATORY REVIEWS (2008) 9, 51–54

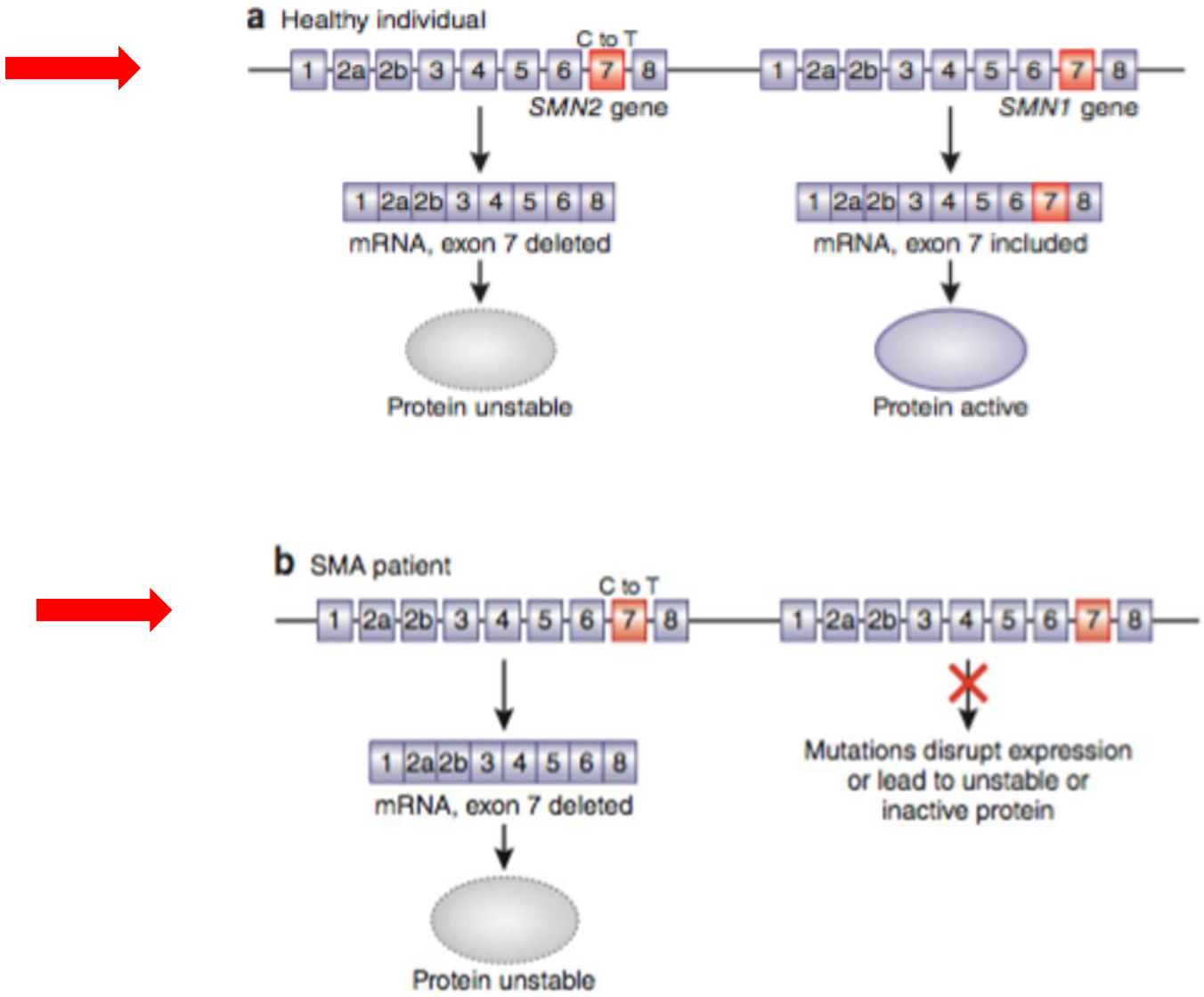
Paediatric Respiratory Reviews

REVIEW

The use of invasive ventilation is appropriate in children with genetically proven spinal muscular atrophy type I: the motion against

Monique M. Ryan*

Neurosciences Department, Royal Children's Hospital and Murdoch Children's Research Institute, Melbourne, Australia



US National Library of Medicine. Genetics Home Reference: spinal muscular atrophy. 2017.

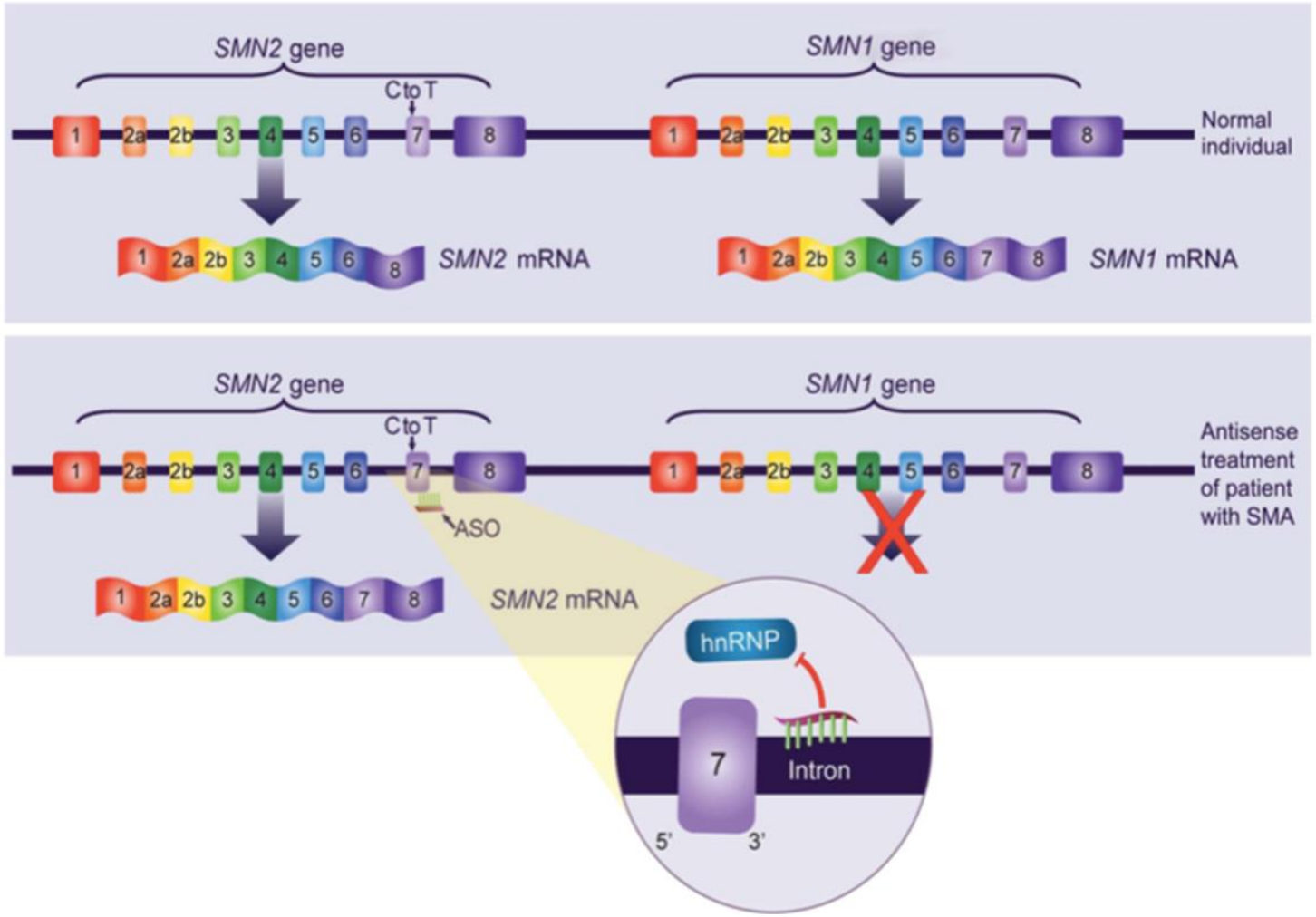
NUSINERSEN

Features and properties of nusinersen	
Alternative names	ISIS 396443; ISIS-SMN_{Rx}
Class	Antisense oligonucleotides; spinal muscular atrophy gene therapies
Mechanism of action	Increases the inclusion of exon 7 in *SMN2* mRNA transcripts and thus the production of full-length SMN protein
Route of administration	Intrathecal
Pharmacodynamics	Binds to a specific sequence in the intron, downstream of exon 7 on the *SMN2* pre-mRNA, thereby modulating the splicing of the *SMN2* mRNA transcript to include exon 7 and enhancing the production of full-length SMN protein
Pharmacokinetics	Distributed from the site of administration (CSF) into motor neurons throughout the CNS; cleared from the CSF into the systemic circulation consistent with normal CSF turnover; CSF concentrations still quantifiable 15–168 days after dosing, indicating prolonged CSF and CNS tissue exposure; median time to C_{max} values ranged from 1.7–6.0 h; estimated mean terminal elimination half-life is 135–177 days (CSF) and 63–87 days (plasma)
Most frequent adverse events	Lower respiratory infection, upper respiratory infection, constipation
ATC codes	
WHO ATC code	N07 (other nervous system drugs)
EphMRA ATC code	N7 (other CNS drugs)
Chemical name	RNA, [2'-*O*-(2-methoxyethyl)](*P*-thio)(m5U-m5C-A-m5C-m5U-m5U-m5U-m5C-A-m5U-A-A-m5U-G-m5C-m5U-G-G)

C_{max} maximum plasma concentration, *CSF* cerebrospinal fluid, *CNS* central nervous system, *mRNA* messenger ribonucleic acid, *SMN* survival motor neuron

Sheridan M. Hoy. Nusinersen: First Global Approval. Drugs. 2017.

NUSINERSEN



Chiriboga CA, Swoboda KJ, Darras BT, et al. Results from a phase 1 study of nusinersen (ISIS-SMN(Rx)) in children with spinal muscular atrophy. Neurology. 2016