

ERT IN JUVENILE AND ADULT GLYCOGENOSIS TYPE 2

Bruno Bembi - Giovanni Ciana - Andrea Dardis

**Unità di Malattie Metaboliche-Laboratorio di Malattie Rare
Istituto per l'Infanzia "Burlo Garofolo"
Trieste - Italy**

Glycogenosis type II, Pompe disease or acid maltase deficiency

- Autosomal recessive lysosomal storage disease
- Deficit of α -glucosidase or acid maltase
- Glycogen accumulation within the lysosomes leads to enlargement of cardiac and skeletal muscle

Glycogenosis type II

Phenotypic continuum

Infantile onset

- Rapidly progressive muscle weakness
- Cardiomegaly and cardiomyopathy
- Moderate hepatomegaly
- Macroglossia
- Feeding difficulties
- Frequent respiratory infections
- Respiratory distress
- Delayed motor milestones
- Markedly elevated CK
- Rapidly progressive disease course
- no GAA activity



Late onset

- Progressive muscular weakness
- No cardiac involvement
- Swallowing difficulty
- Frequent respiratory infections
- Respiratory distress
- Exercise intolerance
- Elevated CK
- Moderate hepatomegaly
- Residual GAA activity

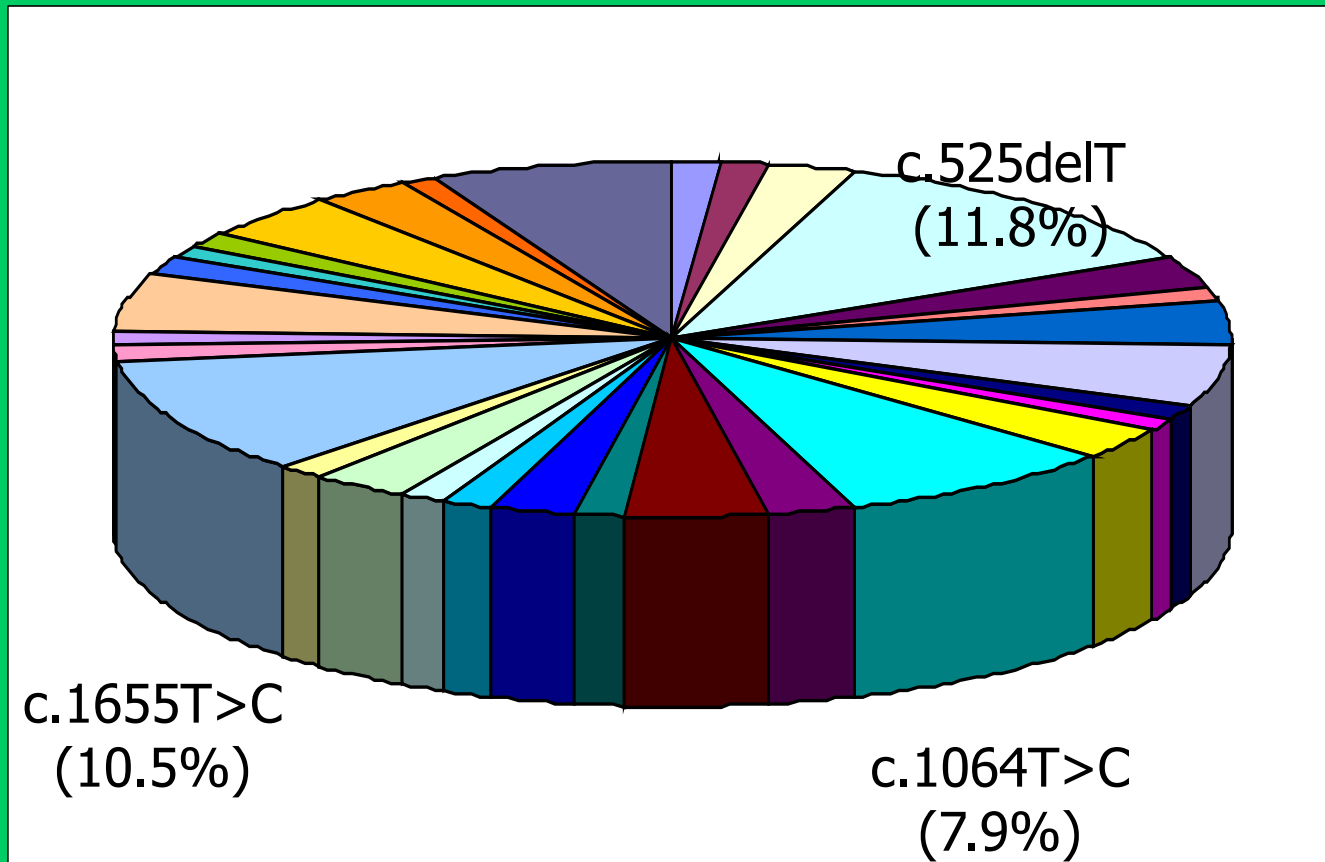
Molecular diagnosis

Genomic DNA amplification

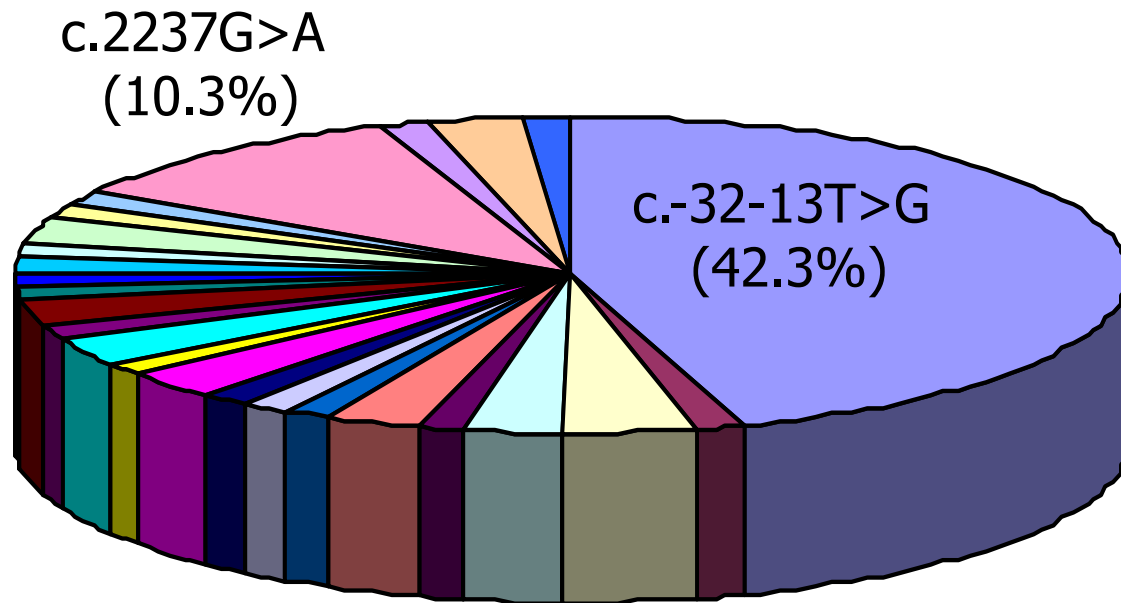
- Screening frequent mutations
- DHPLC
- Direct sequencing

RT-PCR analysis

Allele frequency in the Italian infantile GSDII population



Allele frequency in the Italian late onset GSDII population



Late onset c.-32-13T>G/ c.2237G>A genotype: clinical aspects

Pt# (sex)	Age (years)		First symptoms noted	Mobility status		% enzyme activity	Respiratory follow-up
	onset	Diagnosis		At diagnosis	Follow-up		
1 (F)	13	14	Elevated CK, AST, ALT Lower limb weakness, Fatigue	unrestricted	With help	18 (M)	Reduction of pulmonary function
2 (F)	2	2	Elevated CK, AST, ALT	unrestricted	unrestricted	NA	Normal
3 (F)	30	31	Elevated CK, Fatigue Generalized weakness	unrestricted	With walker or wheelchair	4.3 (L)	Respiratory distress
4 (M)	18	27	Elevated CK, AST, ALT Generalized weakness	unrestricted	With help	10 (M)	non invasive ventilation
5 (F)	30	52	Difficulty in walking up steps Fatigue	unrestricted	With help	absent	Supplemental oxygen
6 (M)	22	46	Generalized weakness Fatigue	unrestricted	With help	0.1 (L)	Reduction of pulmonary function
7 (M)	38	38	Generalized weakness Fatigue	unrestricted	With difficulty	8 (L)	Reduction of pulmonary function
8 (M)	1	2	Elevated CK, AST, ALT Muscular weakness	Impaired ambulation	With wheelchair	3.7 (M)	non invasive ventilation
9 (M)	1	10	Elevated CK, AST, ALT	unrestricted	unrestricted	0.02 (M)	Normal

Enzyme Replacement Therapy

- Juvenile forms: 7 (4 male, 3 female, age 12-18 yrs)
- Adult forms: 6 (3 male, 3 female; age 27-54)

Myozyme dosage:
20 mg/kg/every two weeks

Treatment period:
12 to 24 months

Clinical symptoms

	Juveniles	Adults
Tracheotomy	1/7	2/6
Assisted ventilation	2/7	4/6
Severe hypotonia	2/7	5/6
Wheelchair	1/7	2/6
Reduced/impaired motility	4/7	6/6
Lordosis-scoliosis	3/7	5/6
Muscle pain	3/7	2/6
Headache	2/7	6/6

Residual enzyme activity: 2.8-10%

Efficacy evaluation: clinical parameters

Respiratory parameters

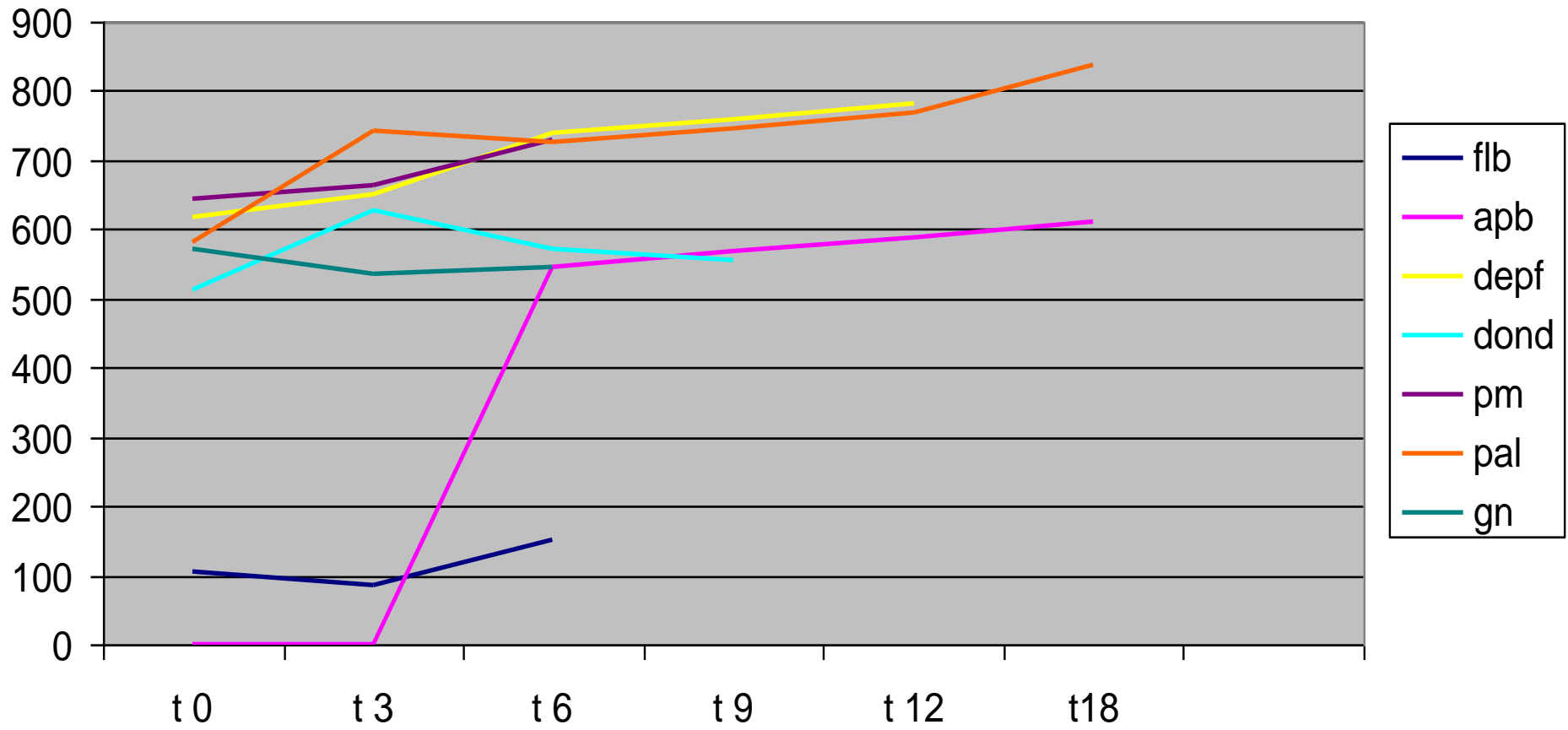
	Juveniles		Adults	
	T0	T > 12	T0	T > 12
tracheotomy	1	-	2	-
Ventilatory support	2	1	4	4 Reduced time
PCO ₂ > 40 mmHg	5	2	6	4

Efficacy evaluation: clinical parameters

	Juveniles	Adults
	T 12 -24	T 12 -24
Muscular strenght	Improved: 7/7	Improved: 6/6
Fatigue	Reduced: 4/4	Reduced: 5/6
Mobility	Improved: 4/4	Improved: 6/6
Muscle pain	0/3	1/6
Headache	0/2	1/6

No need of life-saving procedures

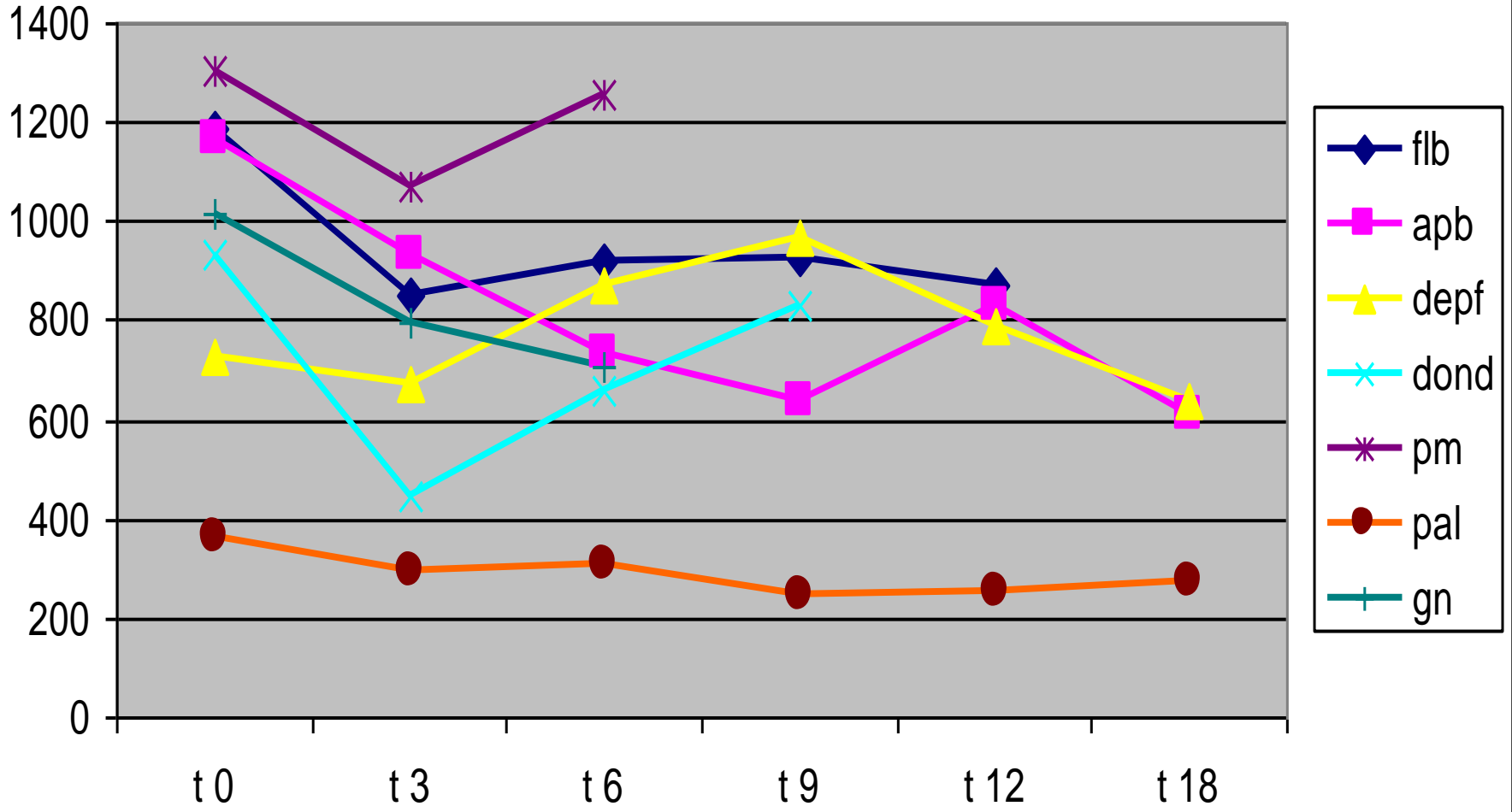
6 Minute Wolking Test



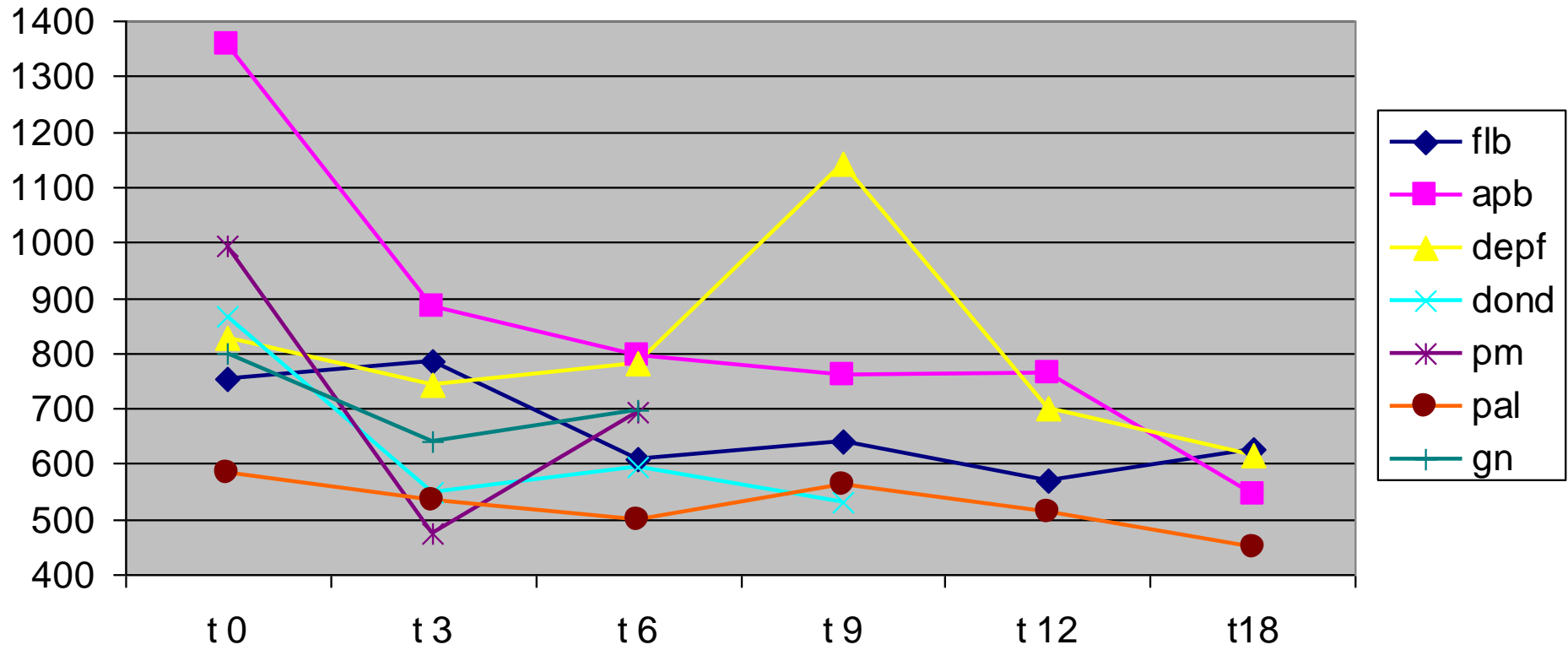
Efficacy evaluation: laboratory and instrumental parameters

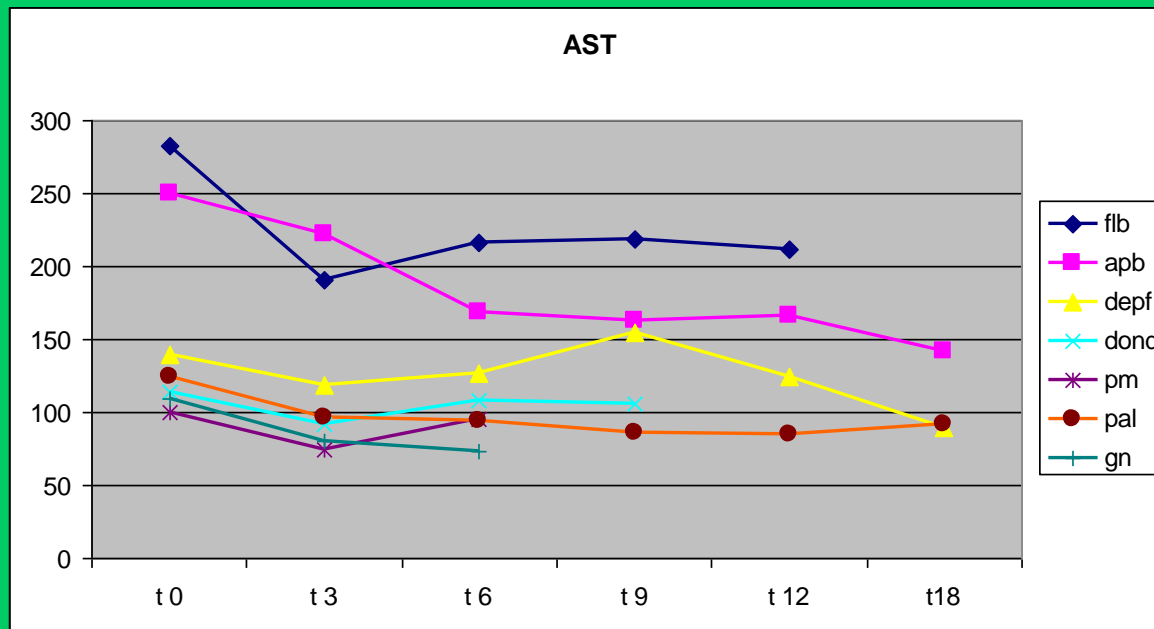
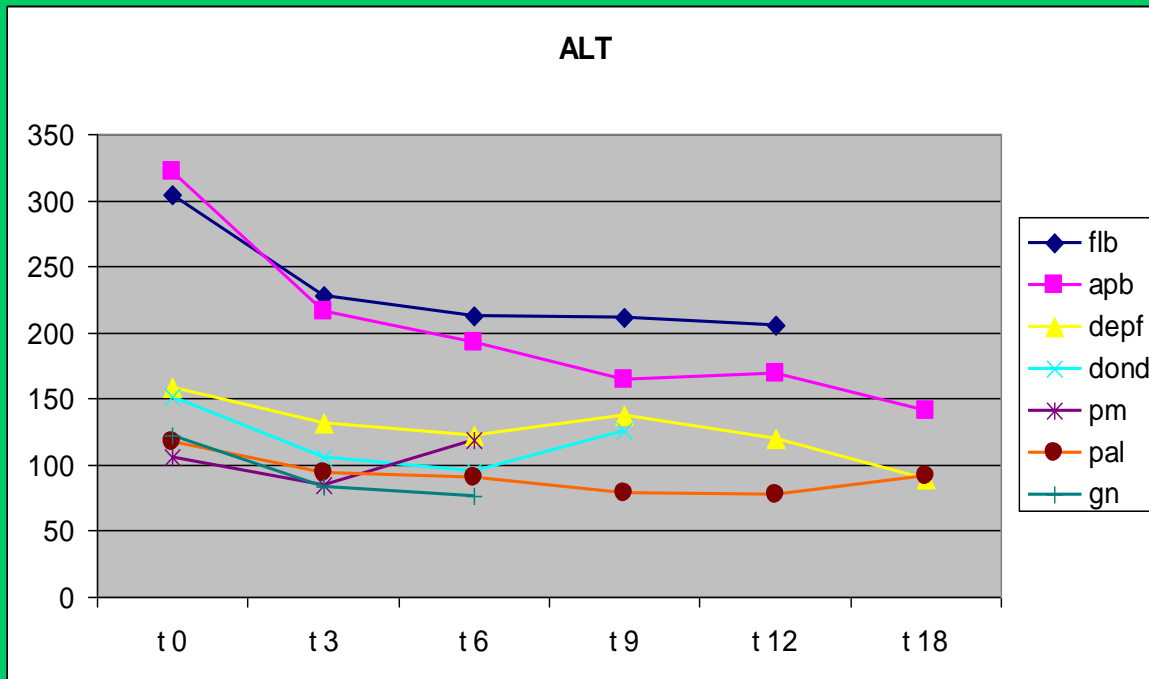
- CK, LDH, AST, ALT modifications
- Plasmatic creatinine
- Urinary oligosaccharides
- Muscular biopsy: histochemical and EM variations
- Imaging: muscular MNR

CPK

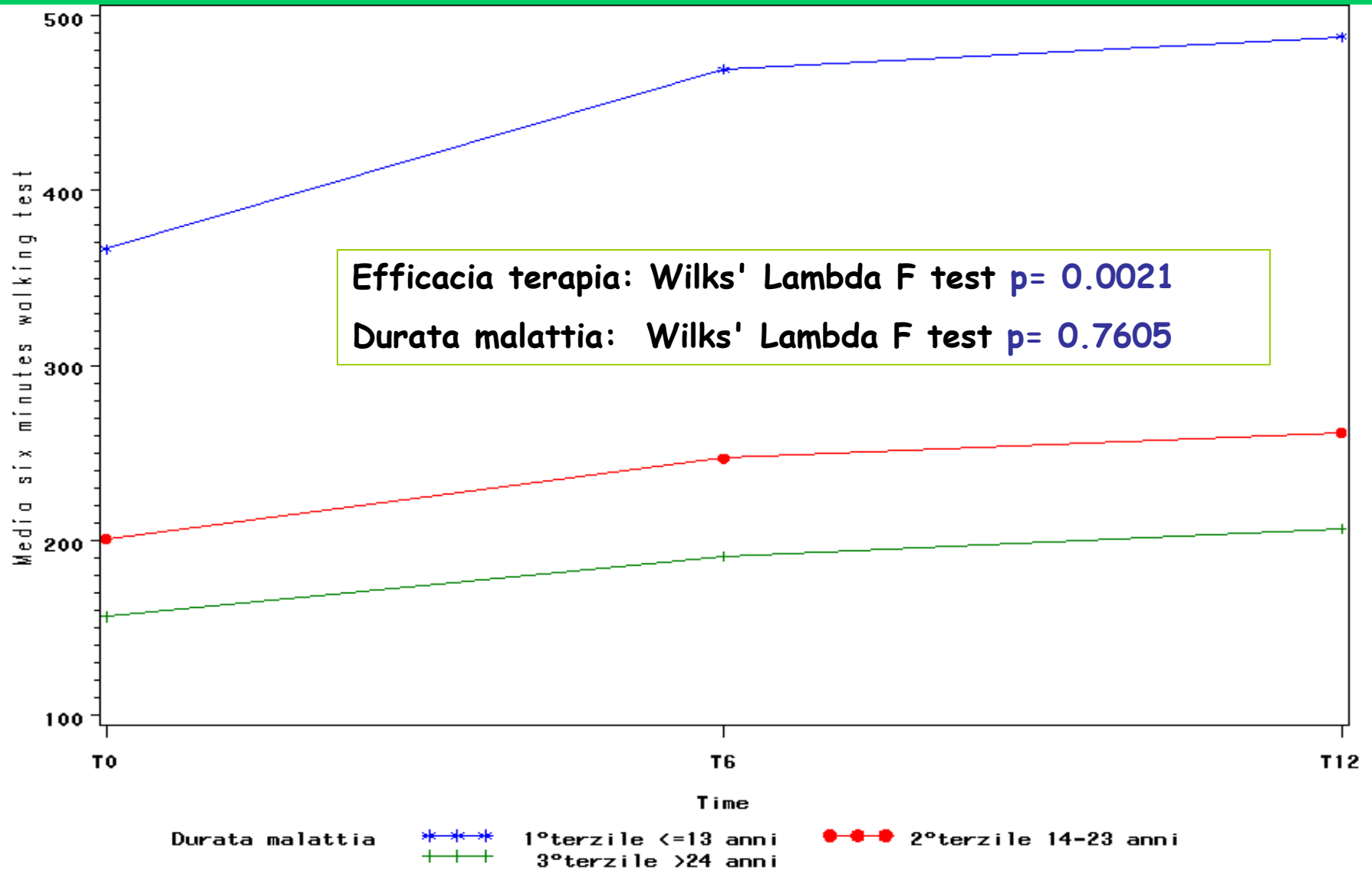


LDH

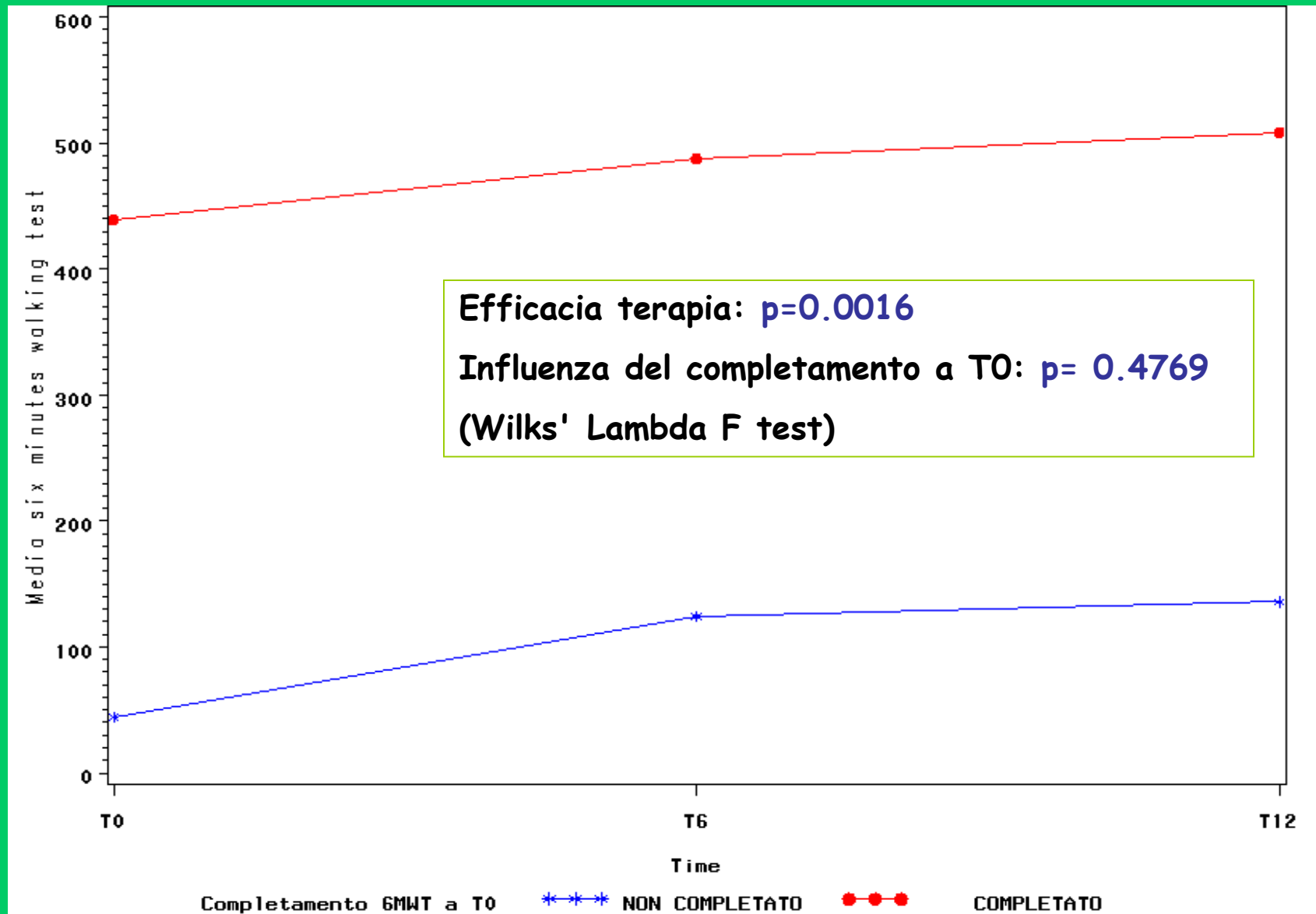




RELAZIONE TRA INCREMENTO DEL 6 MINUTES WALKING TEST E DURATA DELLA MALATTIA A TO



RELAZIONE TRA INCREMENTO DEL 6mwt E SUO COMPLETAMENTO A T0



**EFFICACIA DELLA ERT SULLA SINTOMATOLOGIA DOLOROSA
(29 pazienti: 7 in età pediatrica, 22 adulti)**

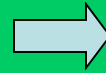
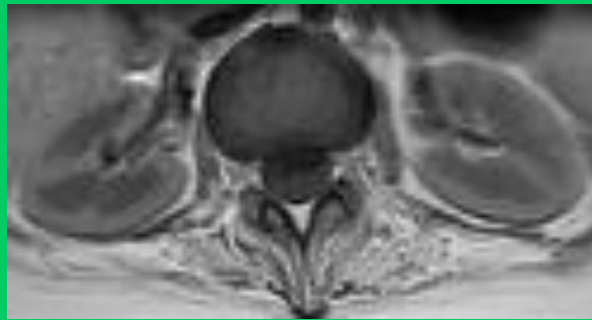
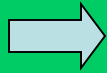
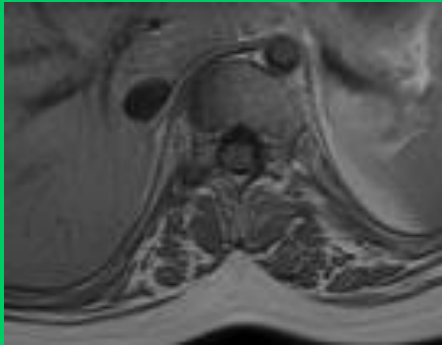
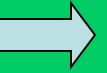
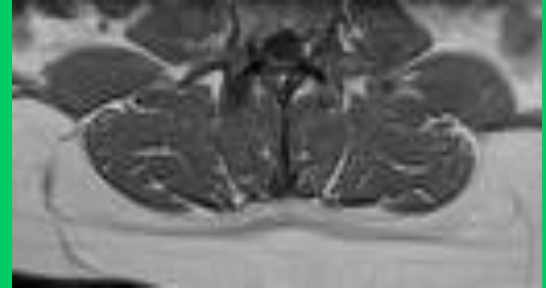
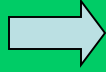
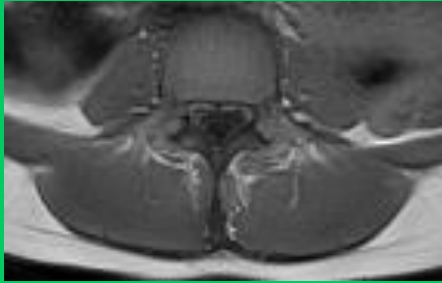
	presente		assente		p (two sided exact binomial test)
	N	%	N	%	
Cefalea					
T0	8	27.6	21	72.4	0.0122
T12	2	6.9	27	93.1	
Dolore muscolare					
T0	11	37.9	18	62.1	0.0020
T12	3	10.3	26	89.7	

VARIAZIONI MEDIE DEI PARAMETRI RESPIRATORI, A 6 E 12 MESI

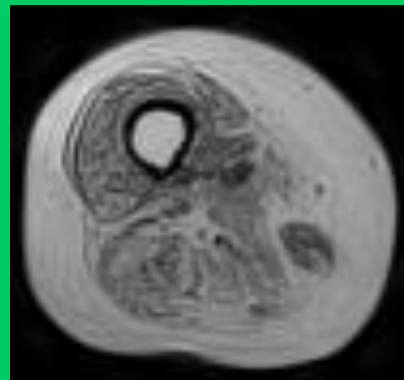
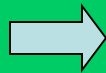
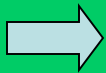
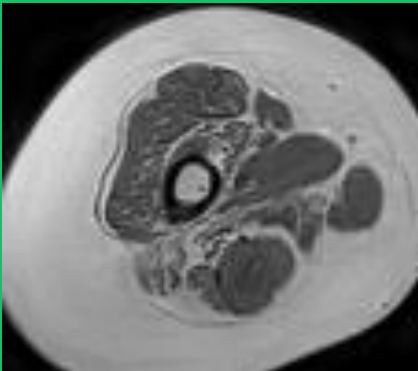
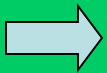
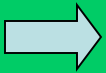
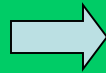
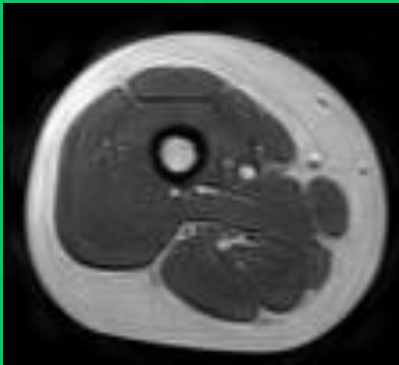
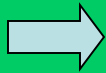
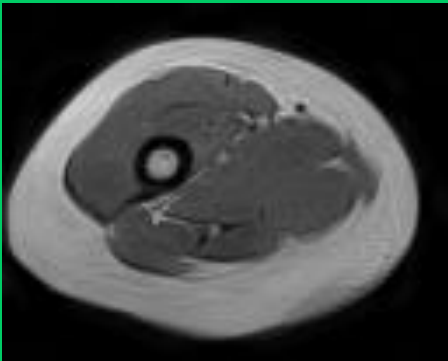
	N pazienti	Incremento medio	95%CI	range	p
PCO2					
T0 - T6	22	-2.5	-5.4 - 0.4	-19.6 - 7.0	0.2863
T6 - T12	23	-3.2	-5.5 -0.9	-15.6 - 9.0	0.0043
T0 - T12	25	-5.1	-8.7 -1.5	-28.5 - 3.9	0.0347
VC					
T0 - T6	28	0.4	-3.5 - 4.4	-36.0 - 28	0.1516
T6 - T12	28	0.7	-1.3 - 2.8	-11.0 - 13	0.8318
T0 - T12	29	1.1	-3.2 - 5.3	-38.5 - 27	0.7011
FEV 1					
T0 - T6	20	0.23	0.07 - 0.37	-0.27 - 1.22	0.0044
T6 - T12	20	0.05	-0.05 - 0.15	-0.48 - 0.44	0.3593
T0 - T12	27	0.16	0.05 - 0.27	-0.33 - 0.72	0.0755

**OPEN PROBLEMS IN PRE-ADOLESCENT
SEVERE JUVENILE PATIENTS**

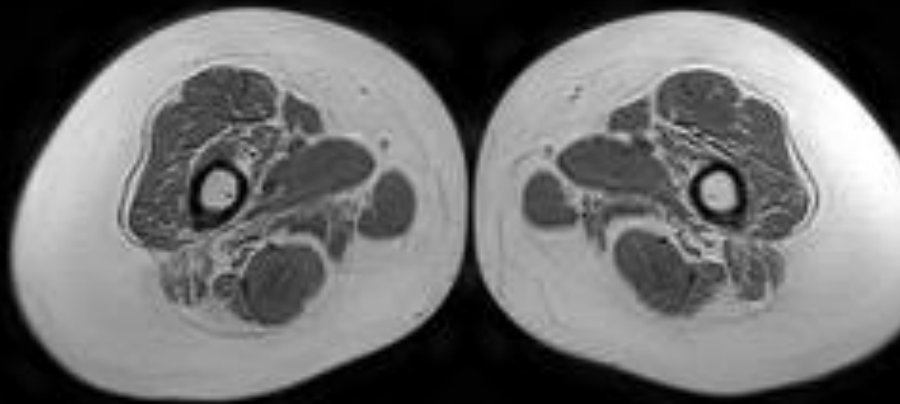
IMAGING



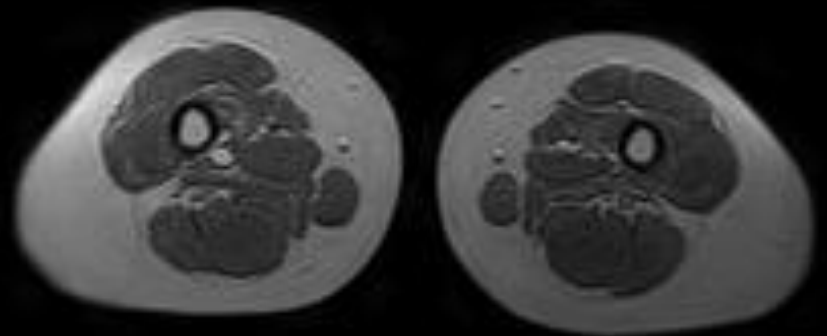
IMAGING



FBL: born 04.1993

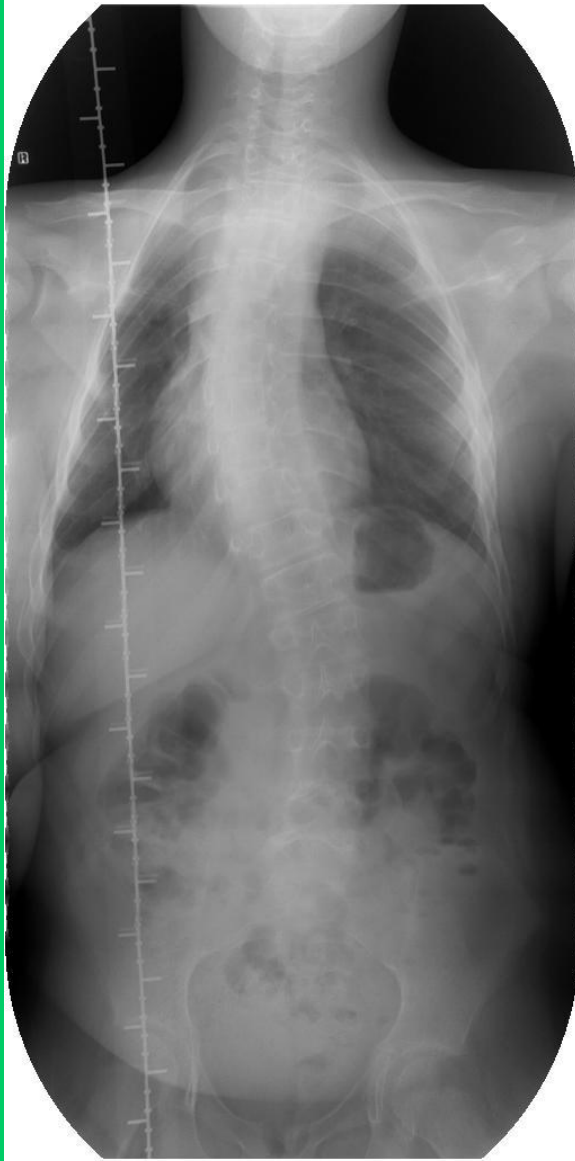


May 2006

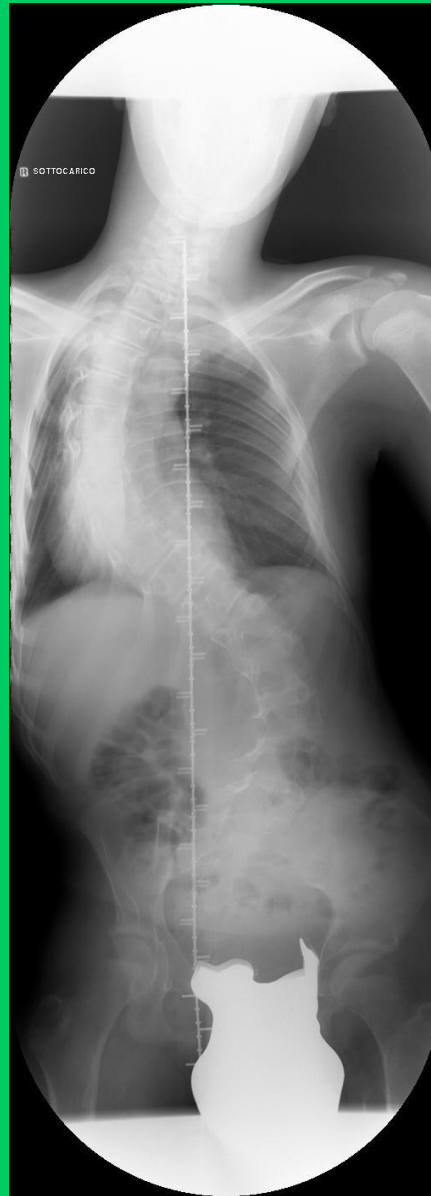


May 2007

FBL: born 04.1993



Jan 2005



March 2007



July 2007

**Coordinamento Regionale
Malattie Rare, AOU-
Udine**

**Unità di Malattie
Metaboliche
IRCCS Burlo Garofolo**

**Giovanni Ciana
Andrea Dardis
Roberta Cariati
Riccardo Addobbati,
Marco Nevyjel
Silvia Dominissini
Stefania Zampieri**

Maria Gabriela Pittis

- **All patients and families**
- **AIG**

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