Additional file 1:

Supplementary table 1. Search syntax used in different databases to gather the bibliographic data.

1. Pubmed: (("Mucopolysaccharidosis"[All Fields] AND "II"[All Fields]) OR "Mucopolysaccharidosis II"[All Fields] OR "MPS II"[All Fields] OR "Hunter syndrome"[All Fields]) AND ("idursulfase"[All Fields] OR "enzyme replacement therapy"[All Fields] OR "ert"[All Fields]) OR "iduronate-2-sulphatase"[All Fields] AND ("case reports"[Publication Type] OR "case"[All Fields] OR "report"[All Fields])
2. Embase: 'hunter syndrome' AND ('enzyme replacement' OR 'iduronate 2 sulfatase' OR 'idursulfase') AND ('case report' OR 'case study' OR 'medical record review')
3. Cochrane: (“Mucopolysaccharidosis II” OR "Hunter syndrome") AND (“enzyme replacement” OR idursulfase OR “iduronate-2-sulphatase”)
4. LYLACS (webpage: http://lilacs.bvsalud.org/es/): (Title, Summary, Issue) “mucopolysaccharidosis II” and “"enzyme replacement”

Supplementary table 2. Case reports of males with MPS-II published prior to the bibliographic search of meta-analysis of clinical studies (January 2008 to December 2015).

Reference Publication Included in Bradley study.	(Severe or attenuated) Mutations	Age at diagnosis Age at ERT start ERT duration	Treatment IV Dose Schedule	Outcomes evaluated in Bradley meta-analysis modified (improved or impaired (IRR)) after ERT (Novelties)
Studies published prior to the bibliographic search of the meta-analysis of clinical studies (2008 to December 2015)				
Kim et al, 2014 [1] Journal article Not included	(S) ?	72 months 72 months 15 months	Idursulfase 0.5 to 1 mg/kg/weekly	**uGAGs; LiverV**; 6MWT or endurance; pulmonary function; **antibodies**. (Immune modulation protocol)
NoH et al, 2014 [2] Letter to editor Not included	(?) ?	72 months 72 months 4 months	Idursulfase 0.5 mg/kg/weekly	(Skin lesions decrease after ERT)
Lampe et al, 2014 [3] Journal article 1 MPS-II *Included*	(?) p.R88H mutation	Pre-natal 0.3 months 2.3 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs.** (Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article 1 MPS-II *Included*	(?) p.R95G mutation	1 week 1.4 months 22.6 months	Idursulfase 1.5 to 0.5 mg/kg/weekly	**LiverV** (Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article 1 MPS-II *Included*	(?) p.P86L mutation	6 weeks 2 months 2.3 months	Idursulfase 0.6 to 0.5 mg/kg/weekly	**uGAGs.** (Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article *Included*	(?) p.R493P mutation	1 day 2.3 months 36 months	Idursulfase 0.6 to 0.5 mg/kg/weekly	**uGAGs;** LiverV; 6MWT or endurance; Growth (Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article *Included*	(?) c.1270insCC	4 weeks 2.5 months 5 years	Idursulfase 0.5 mg/kg/weekly	**uGAGs;** LiverV. (Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article *Included*	(?) p.G336E	11 weeks 2.8 months 17 months	Idursulfase 0.5 mg/kg/weekly	**LiverV.** (Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article *Included*	(?) c.1133A>G	1 week 6 months 4 years	Idursulfase 0.5 mg/kg/weekly	(Safety and efficacy evaluation of ERT)
Lampe et al, 2014 [3] Journal article *Included*	(?) c.1362-1365dup	5.5 months 6.5 months 4 years	Idursulfase 0.66 to 0.5 mg/kg/weekly	**uGAGs;** LiverV. (Safety and efficacy evaluation of ERT)
Christianto et al, 2013 [4] Journal article Not included	(S) c.1053delT in exon 8	6 years 27 years 12 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs; LiverV**; 6MWT or endurance; **antibodies**. (Safety and efficacy evaluation of ERT)
Volpi et al, 2013 [5] Journal article Not included	(S) P120R mutation on Xq28	2 years and 9 m. 3 years 10 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs** (Study of plasmatic

Reference Publication Included in Bradley study.	(Severe or attenuated) Mutations	Age at diagnosis Age at ERT start ERT duration	Treatment IV Dose Schedule	Outcomes evaluated in Bradley meta-analysis modified (improved or impaired (IRR)) after ERT (Novelties)
				dermatan sulfate (DS) during ERT)
Sato et al, 2013 [6] Journal article Not included	(S) ?	3 years 7 years 24 months	Idursulfase 0.5 mg/kg/weekly	(Limited efficacy for cardiac valve disease of ERT)
Tajima et al, 2013 [7] Journal article *Included*	(S) Recombination IDS gene and the IDS-2 pseudogene	3 years 3 years 34 months	Idursulfase 0.3 - 0.5 mg/kg/weekly	**uGAGs; LiverV** (Safety and efficacy evaluation of ERT)
Tajima et al, 2013 [7] Journal article *Included*	(S) Recombination IDS gene and the IDS-2 pseudogene	4 months 4 months 32 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs;** (Safety and efficacy evaluation of pre-symptomatic initiation of ERT)
Puiu M et al, 2013 [8] Journal article Not included	(S) ?	3 years 3 years and 3 m. 1 year	Idursulfase 0.5 mg/kg/weekly	**LiverV**; 6MWT; JROM; Growth; QoL; Sleep apnea. (Improvement of cognitive and conductual functioning after ERT)
Marín LL et al, 2012 [9] Short report Not included	(A) ?	6 years 9 years 9 months	Idursulfase 0.5 mg/kg/weekly	(Improvement of skin lesion after ERT)
Hoffmann B et al, 2011 [10] Journal article Not included	(A) A85T, missense mutation	8 years ? 20 months	Idursulfase 0.5 mg/kg/weekly	LiverV; 6MWT or endurance; **Growth;** QoL; (Safety and efficacy evaluation of ERT)
Hoffmann B et al, 2011 [10] Journal article Not included	(S) missense mutation C184F	5 years ? 22 months	Idursulfase 0.5 mg/kg/weekly	LiverV; 6MWT or endurance; **Growth;** QoL; (Safety and efficacy evaluation of ERT)
Hoffmann B et al, 2011 [10] Journal article Not included	(S) 131del10, frame-shift mutation	5 years ? 31 months	Idursulfase 0.5 mg/kg/weekly	6MWT or endurance; **Growth;** QoL; (Safety and efficacy evaluation of ERT)
Tylki-Szymanska et al, 2012 [11] Journal article *Included*	(¿) missense mutationc.1568 A>G in exon 9 of the IDS gene	3 months 3 months 36 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs;** (Safety and efficacy evaluation of ERT)
Papadia F et al, 2011 [12] Journal article Not included	(S) Splice site mutation(c.418+1 G>C).	3 years 4 years ant 10 m. 3 years	Idursulfase 0.5 mg/kg/weekly	**uGAGs; LiverV; JROM**; (Early use of ERT improve bone abnormalities)
Pérez-Calvo et al, 2011[13] Journal article Not included	(A) un genotipo R443/X	18 months 30 years 6 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs; 6MWT; JROM**; QoL; **antibodies**. (The JROM in later stages of disease may benefit from ERT)
Tchan MC et al, 2011 [14] Journal article	(A) ?	20 years 44 years 12 months	Idursulfase 30 mg/weekly	**uGAGs; 6MWT;** QoL. (Safety and efficacy

Reference Publication Included in Bradley study.	**(Severe or attenuated) Mutations**	**Age at diagnosis Age at ERT start ERT duration**	**Treatment IV Dose Schedule**	**Outcomes evaluated in Bradley meta-analysis modified (improved or impaired (IRR)) after ERT (Novelties)**
Not included				evaluation of ERT in adult age)
Tchan MC et al, 2011 [14] Journal article Not included	(A) ?	26 years 51 years 12 months	Idursulfase 36 mg/weekly	**uGAGs; 6MWT**; QoL. (Safety and efficacy evaluation of ERT in adult age)
Tchan MC et al, 2011 [14] Journal article Not included	(A) ?	22 years 46 years 12 months	Idursulfase 36 mg/weekly	**uGAGs;** QoL; **IRR.** (Safety and efficacy evaluation of ERT in adult age)
Wang RY et al, 2009 [15] Journal article Not included	(A) homozygous P533R IDUA mutations	3 years and 9 m. 3 years and 11 m. 2 years and 6 m.	Idursulfase 0.5 mg/kg/weekly	**uGAGs;** (Evaluate central nervous system effects in MPS II patients)
Wang RY et al, 2009 [15] Journal article Not included	(A) IDS mutation, hemizygous R8X mutation	4 years and 7 m. 4 years and 11 m. ?	Idursulfase 0.5 mg/kg/weekly	**uGAGs;** (Evaluate central nervous system effects in MPS II patients)
Galán Gómez E et al, 2008 [16] Letter to editor Not included	(S) I2S gene showed an N350H mutation in exon 8	7 months 3 years 27 weeks	Idursulfase 0.5 mg/kg/weekly	**uGAGs; Liver;** 6MWT; **antibodies**. (The JROM in later stages of disease may benefit from ERT)
Westhoff M et al, 2011 [17] Journal article Not included	(A) ?	3 years 37 years 24 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs; 6MWT; JROM; pulmonary function;** (ERT benefits adult Hunter patients in restrictive ventilatory defects.)
Sanchez JI et al, 2015 [18] Congress Not included	? ?	? ? ?	Idursulfase ? ?	(ERT improve macular edema in MPS-II patient.)
Gkavogiannakis N et al, 2015 [19] Congress 1 MPS-II Males	(A) ?	34 years ? ?	Idursulfase ? ?	**IRR; antibodies.** (Successful desensitization procedure to idursulfase.)
Fischer et al, 2015 [20] Congress Not included	? ?	? 4 years ?	Idursulfase ? ?	(Idursulfase did not precipitate/worsen autoimmune anemia or thrombocytopenia)
Lau HA et al, 2015 [21] Congress Not included	(A) ?	? 35 years 21 months	Idursulfase ? ?	(ERT did not prevent progression of vision loss)
Kinoshita M et al, 2014 [22] Congress Not included	(A) ?	5 years 20 years ?	Idursulfase ? ?	(ERT improves cortical function but aggravated epileptogenic.)

Reference Publication Included in Bradley study.	(Severe or attenuated) Mutations	Age at diagnosis Age at ERT start ERT duration	Treatment IV Dose Schedule	Outcomes evaluated in Bradley meta-analysis modified (improved or impaired (IRR)) after ERT (Novelties)
Bivina L et al, 2014 [23] Congress Not included	? ?	6 years 6 years 4 years	Idursulfase ? ?	(Early ERT and transplant slowed progression of the disease)
Bivina L et al, 2014 [23] Congress Not included	? ?	2.5 years 2.5 years 8.5 years	Idursulfase ? ?	(Early ERT and transplant slowed progression of the disease)
Bivina L et al, 2014 [23] Congress Not included	? ?	Pre-nataly 4 months ?	Idursulfase ? ?	Growth; developmental improvements (Early ERT and transplant slowed progression of the disease)
Nava E et al, 2012 [24] Journal article Not included	(S) complete exon 7 deletion in the iduronate 2-sulfatase gene	2 years and 4 m. 4 years and 9 m. 2 years and 1 m.	Idursulfase ? ?	6MWT; **JROM;** (Botulinum Toxin for the Treatment of Equinus Deformity in MPS-II Patients)
Nava E et al, 2012 [24] Journal article Not included	(S) ?	1 year and 1 m. 6 years and 6 m. 3 years	Idursulfase ? ?	(Botulinum Toxin for the Treatment of Equinus Deformity in MPS-II Patients)
Bonanni P et al, 2012 [25] Journal article Not included	(S) ?	1 year and 7 m. 8 years and 3 m. 14 months	Idursulfase ? ?	(Epilepsy may be a treatable cause of neurological regression in individuals with MPS II)
Uz B et al, 2012 [26] Letter to editor Not included	(A) ?	Newborn period 10 years and 2 m. 8 months	Idursulfase 0.5 mg/kg/weekly	(Hunter syndrome and new onset idiopathic thrombocytopenic purpura)
Farooq MU et al, 2008 [27] Letter to editor Not included	? IDS gene, a (A>T) change at nucleotide 595	2 year 11 years and 6 m. 12 months	Idursulfase 0.5 mg/kg/weekly	Liver; pulmonary function; (Novel mutation in the Iduronate 2 sulfatase gene resulting in MPS-II and Chorea.)
Farooq MU et al, 2008 [27] Letter to editor Not included	? IDS gene, a (A>T) change at nucleotide 595	4 years 13 years 12 months	Idursulfase 0.5 mg/kg/weekly	Liver; pulmonary function; (Novel mutation in the Iduronate 2 sulfatase gene resulting in MPS-II and Chorea.)

?:No data in the study´s paper; 6MWT: 6-minute walk test; Cardiac (ECHO): Cardiac evaluation with echocardiogram; IRR: infusion-related reaction; IV: Intra-venous; JROM; joint range of motion; MPS-II: Mucopolysaccharidosis type II; QoL: Quality of life; SOE: Strenght of evidence; uGAGs: Urinary glycosaminoglycans.

Supplementary table 3. Case reports of males with MPS-II published later to the bibliographic search of the meta-analysis of clinical studies (January 2016 to April 2018).

Reference Publication	(Severe or attenuated) Mutations	Age at diagnosis Age at ERT start ERT duration	Treatment IV Dose Schedule	Outcomes evaluated in Bradley meta-analysis modified (improved or impaired (IRR)) after ERT (Novelties)
Studies published later to the bibliographic search of the meta-analysis of clinical studies (January 2016 to April 2018).				
Kim et al, 2017 [28] Journal article	(S) ?	14 months 15 months 5 years	Idursulfase 0.5 to 1 mg/kg/weekly	**uGAGs;** 6MWT or endurance; JROM; pulmonary function; **antibodies**. (uGAGs as biomarker for antibodies; Anti-immunological scheme)
Ngu et al, 2017 [29] Journal article	(A) c.1608_1609delTA (p.Tyr536Ter) mutation exon 9 IDS gene	6 years 11 years 20 / 24 months	Idursulfase / idursulfase beta 0.5 / 1.67 to 0.5 mg/kg/weekly	**uGAGs; LiverV**; **6MWT**; growth; **Cardiac (ECHO);** sleep disorder; **antibodies**. (idursulfase beta after idursulfase as Anti-immunological scheme)
Nishiyama et al, 2016 [30] Journal article	(A) ?	6 years 6 years 18 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs;** LiverV; Spleen Volume; JROM; sleep disorder. (Hydroneprhosis resolution)
Gupta et al, 2014 [31] **& Madireddi et al, 2016** [32] Journal article	(A) mutation A85T caused by a G to A substitution at nucleotide position c.253 in the exon 3 of IDS	24 years 24 years 4 months	Idursulfase 0.5 mg/kg/weekly	**Spleen Volume; 6MWT;** JROM; pulmonary function; QoL. (Diagnosis of MPS-II by enzyme assay and mutational analysis)
Akiyama R et al, 2018 [33] Congress	(A) ?	12 years 12 years ? months	Enzyme replacement therapy	Growth (Optic abnormalities not changed by ERT treatment)
Al B et al, 2017 [34] Journal article	(S) ?	10 days 10 days 1.4 months	Idursulfase 0.5 mg/kg/weekly	**uGAGs.** (hematopoietic stem cell transplantation (HSCT))
Jarstad A eta al, 2017 [35] Congress	(A) ?	35 years 39 years 4 years	Enzyme replacement therapy	(Optic abnormalities not changed by ERT)
Moreno KJ et al, 2017 [36] Congress	(A) hemizygous mutation in intron	25 years 25 years 6 months	Idursulfase 0.5 mg/kg/weekly	**Cardiac (ECHO)**; QoL.

Reference Publication	(Severe or attenuated) Mutations	Age at diagnosis Age at ERT start ERT duration	Treatment IV Dose Schedule	Outcomes evaluated in Bradley meta-analysis modified (improved or impaired (IRR)) after ERT (Novelties)
	5 of the IDS gene, c.709-658GN A.			(Cardiac improvement after ERT)
Bettocchi I et al, 2016 [37] Congress	(S) IDS gene deletion of exons 1-7, extending to regions Xq28 e Xq27.3, removing the entire pseudogene IDS2 and genes FMR1 and AFF2	3 months 18 months 35. years	Idursulfase 0.5 mg/kg/weekly	(MPS-II mutation analysis)
Romero FHC et al, 2016 [38] Congress	(S) IDS/IDSP1 inversion	3 years ? months 3 years	Idursulfase 0.5 mg/kg/weekly	**IRR.** (Adverse events under Idursulfase treatment)
Romero FHC et al, 2016 [38] Congress	(S) IDS/IDSP1 inversion	36 months ? months 2 years	Idursulfase 0.5 mg/kg/weekly	**IRR.** (Adverse events under Idursulfase treatment)
Romero FHC et al, 2016 [38] Congress	(S) IDS/IDSP1 inversion	3 years ? months 5 years	Idursulfase 0.5 mg/kg/weekly	**IRR.** (Adverse events under Idursulfase treatment)

?:No data in the study´s paper; 6MWT: 6-minute walk test; Cardiac (ECHO): Cardiac evaluation with echocardiogram; IRR: infusion-related reaction; IV: Intra-venous; JROM; joint range of motion; MPS-II: Mucopolysaccharidosis type II; QoL: Quality of life; SOE: strenght of evidence; uGAGs: Urinary glycosaminoglycans.

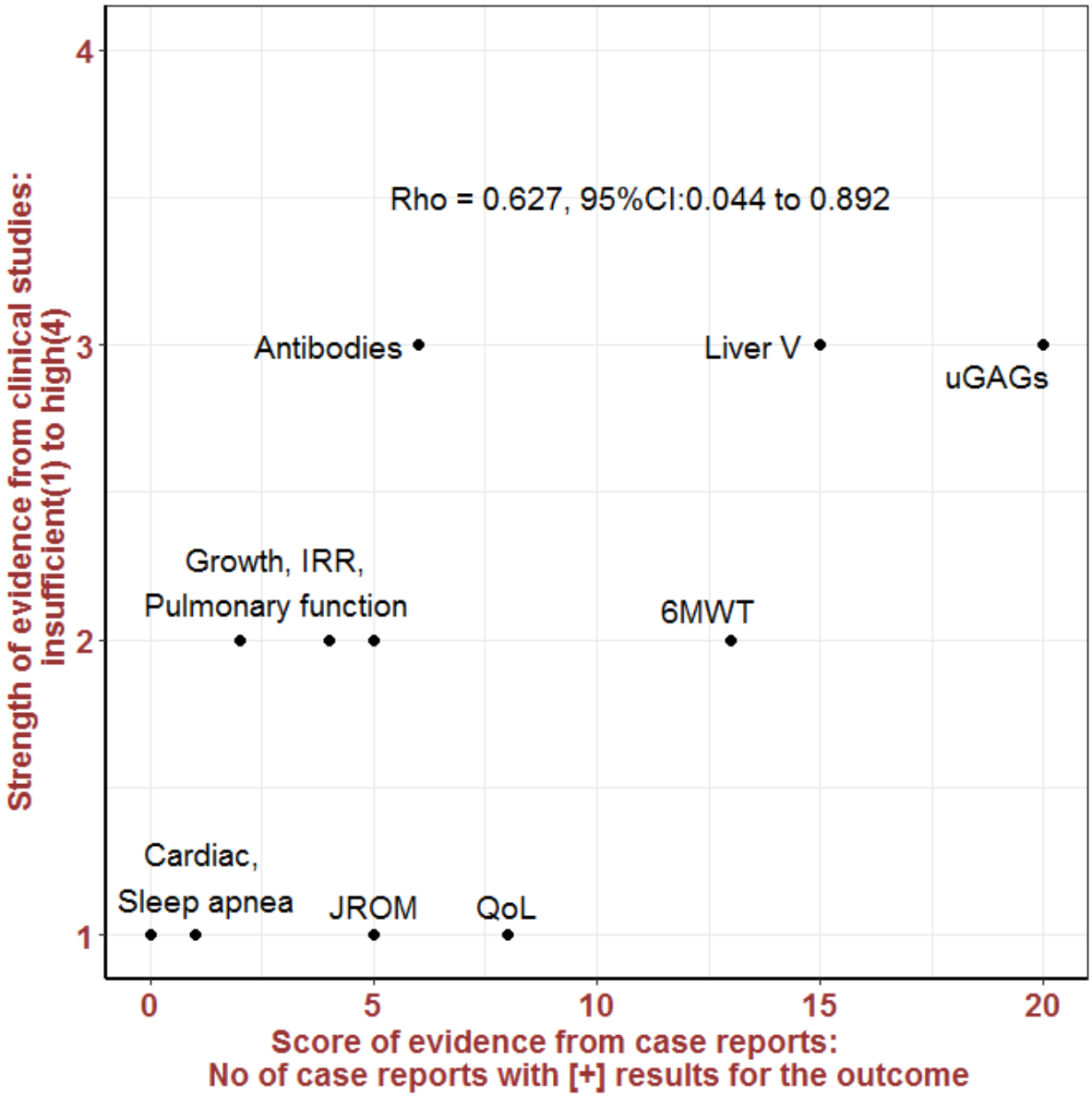
Supplementary table 4. Agreement between the classification of outcomes based on the case report meta-analysis and the SOE classification based on the clinical study meta-analysis. Weak confirmatory method.

	Strength of evidence of clinical study meta-analysis	
Number of case reports [+] for the outcome	**High to moderate**	**Low to insufficient**
≥ 6 [+] of 44 cases **(acceptable evidence group)**	(True positives= 3) -uGAGs -Liver Volume -Antibodies	(False positive=2) -6WMT, QoL,
< 6 [+] of 44 cases **(unacceptable evidence group)**	(False negative=0)	(True negatives=6) - Growth, JROM, Pulmonary function, IRR, sleep apnea, Cardiac.

The 95% confidence interval for the validity index are: positive predictive value: 60% (15 to 95%); negative predictive value: 100% (54 to 100%); sensibility: 100% (29 to 100%) and specificity: 75% (35 to 97%).

6MWT: 6-minute walk test; CI: Confidence interval; IRR: Infusion-related reaction; JROM; Joint range of motion; NPV: Negative predictive value; PPV: Positive predictive value; QoL: Quality of life; Se: Sensitivity; Sp: Specificity; SOE: Strenght of evidence; uGAGs: Urinary glycosaminoglycans.

Supplementary figure 1. Agreement between the score of evidence from the case report meta-analysis and SOE from the clinical study meta-analysis. Weak confirmatory method.



6MWT: 6-minute walk test; CI: Confidence interval; IRR: Infusion-related reaction; JROM: Joint range of motion; QoL: Quality of life; Rho: Spearman correlation coefficient; SOE: Strenght of evidence; uGAGs: Urinary glycosaminoglycans.

Supplementary table 5. Sensitivity analysis on different futility boundaries.

Futility boundary*	True (+/-); False (+/-)	Accuracy%	Se%	Sp%	PPV%	NPV%
5% **	(3/8); (0/0)	100	100	100	100	100
1%	(3/5); (3/0)	73	100	62	50	100
10%	(1/8); (0/2)	82	33	100	100	80
15%	(1/8); (0/2)	82	33	100	100	80
20%	(1/8); (0/2)	82	33	100	100	80
50%	(0/8); (0/3)	73	0	100	0	73

**The analyses were done in primary analysis set: All case reports of males MPS-II treated with ERT that report efficacy and safety. This case reports were written in a narrative form (results not aggregated) and published prior to Bradley bibliographic search.*

*** The futility boundary has been considered the null hypothesis of the analysis.*

6MWT: 6-minute walk test; CI: Confidence interval; NPV: Negative predictive value; PPV: Positive predictive value; Rho: Spearman correlation coefficient; Se: Sensitivity; Sp: Specificity.

REFERENCES

1. Kim KH, Messinger YH, Burton BK. Successful reduction of high-sustained anti-idursulfase antibody titers by immune modulation therapy in a patient with severe mucopolysaccharidosis type II. *Mol Genet Metab Rep.* 2015;2:20-24.
2. Noh TK, Han JS, Won CH, et al. Characteristic "pebbling" skin eruption as a presenting sign of Hunter syndrome. *Int J Dermatol.* 2014;53(12):e594-596.
3. Lampe C, Atherton A, Burton BK, et al. Enzyme Replacement Therapy in Mucopolysaccharidosis II Patients Under 1 Year of Age. *JIMD Rep.* 2014;14:99-113.
4. Christianto A, Watanabe H, Nakajima T, Inazu T. Idursulfase enzyme replacement therapy in an adult patient with severe Hunter syndrome having a novel mutation of iduronate-2-sulfatase gene. *Clin Chim Acta.* 2013;423:66-68.
5. Volpi N, Zampini L, Maccari F, et al. Plasmatic kinetics of dermatan sulfate during enzyme replacement therapy with iduronate-2-sulfatase in a mucopolysaccharidosis II patient. *Glycoconj J.* 2013;30(7):727-732.
6. Sato Y, Fujiwara M, Kobayashi H, Ida H. Massive accumulation of glycosaminoglycans in the aortic valve of a patient with Hunter syndrome during enzyme replacement therapy. *Pediatr Cardiol.* 2013;34(8):2077-2079.
7. Tajima G, Sakura N, Kosuga M, Okuyama T, Kobayashi M. Effects of idursulfase enzyme replacement therapy for Mucopolysaccharidosis type II when started in early infancy: comparison in two siblings. *Mol Genet Metab.* 2013;108(3):172-177.
8. Puiu M, Chirita-Emandi A, Dumitriu S, Arghirescu S. Hunter syndrome follow-up after 1 year of enzyme-replacement therapy. *BMJ Case Rep.* 2013;2013.
9. Marín LL, Gutiérrez-Solana LG, Fernández AT. Hunter syndrome: resolution of extensive typical skin lesions after 9 months of enzyme replacement therapy with idursulfase. *Pediatr Dermatol.* 2012;29(3):369-370.
10. Hoffmann B, Schulze-Frenking G, Al-Sawaf S, Beck M, Mayatepek E. Hunter disease before and during enzyme replacement therapy. *Pediatr Neurol.* 2011;45(3):181-184.
11. Tylki-Szymanska A, Jurecka A, Zuber Z, Rozdzynska A, Marucha J, Czartoryska B. Enzyme replacement therapy for mucopolysaccharidosis II from 3 months of age: a 3-year follow-up. *Acta Paediatr.* 2012;101(1):e42-47.
12. Papadia F, Lozupone MS, Gaeta A, Capodiferro D, Lacalendola G. Long-term enzyme replacement therapy in a severe case of mucopolysaccharidosis type II (Hunter syndrome). *Eur Rev Med Pharmacol Sci.* 2011;15(3):253-258.
13. Pérez-Calvo J, Bergua Sanclemente I, López Moreno MJ, Torralba Cabeza M, Amores Arriaga B. [Early response to idursulfase in a 31-year old male patient with Hunter syndrome]. *Rev Clin Esp.* 2011;211(7):e42-45.
14. Tchan MC, Devine KT, Sillence DO. Three Adult Siblings with Mucopolysaccharidosis Type II (Hunter Syndrome): A Report on Clinical

Heterogeneity and 12 Months of Therapy with Idursulfase. *JIMD Rep.* 2011;1:57-64.
15. Wang RY, Cambray-Forker EJ, Ohanian K, et al. Treatment reduces or stabilizes brain imaging abnormalities in patients with MPS I and II. *Mol Genet Metab.* 2009;98(4):406-411.
16. Galán-Gómez E, Guerrero-Rico A, Cáceres-Marzal C, et al. Early response to idursulfase treatment in a 3 year-old boy affected of Hunter syndrome. *Eur J Med Genet.* 2008;51(3):268-271.
17. Westhoff M, Litterst P. Successful noninvasive ventilation and enzyme replacement therapy in an adult patient with morbus hunter. *JIMD Rep.* 2012;5:77-82.
18. Sanchez JI, Ascaso FJ, Perez I, et al. Role of SD-OCT in the follow-up of a patient with macular edema associated with mucopoysaccharidosis type II (Hunter syndrome) undergoingidursulfase enzyme replacement therapy. *Acta Ophthalmologica.* 2015;93.
19. Gkavogiannakis N, Aggelides X, Makris M. Case of infusion reaction to idursulafase and successful re-administration with desensitization. *European Journal of Allergy and Clinical Immunology.* 2015;70:1.
20. Fischer A, Fernandez K, Flores J, Deshpande G, Croke B, Antony R. Autoimmune thrombocytopenia in a patient with hunter syndrome: Should iduronate-2-sulfatase replacement therapy still be considered? *Pediatric Blood and Cancer.* 2015;62.
21. Lau HA NR, Narayana K, Rucker J, Balcer L and Galetta S. Multiplemechanisms of ophthalmologic involvement in attenuated Hunter syndrome: A case report. *Molecular genetics and metabolism.* 2015;114(2):S69.
22. Kinoshita M, Furujo M, Kubo T. EEG evaluation of mucopolysaccharidosis type II after enzyme replacement therapy. *Clinical Neurology.* 2014;54.
23. Bivina L, Boyadjiev SA. Mucopolysaccharidosis type II (MPS II): case report of three affected siblings. *Molecular Genetics and Metabolism.* 2014;111(s27).
24. Nava E, Weber P, Gautschi M, Nuoffer J, Grunt S. Botulinum toxin type A for the t reatment of equinus deformity in patients with mucopolysaccharidosis yype II. *Journal of Child Neurology.* 2012;27(12):5.
25. Bonanni P, Gubernale M, Martinez F, et al. Non-convulsive status epilepticus of frontal origin in mucopolysaccharidosis type II successfully treated with ethosuximide. *Dev Med Child Neurol.* 2012;54(10):961-964.
26. Uz B, Demiroglu H, Ozcebe OI. Hunter syndrome and new onset idiopathic thrombocytopenic purpura in a young patient. *Ann Hematol.* 2012;91(2):303-304.
27. Farooq MU, Balmer SV, DeRoos ST, Houtman KL, Chillag KL. A novel mutation in the iduronate 2 sulfatase gene resulting in mucopolysaccharidosis type II and chorea: case report of two siblings. *Mov Disord.* 2008;23(10):1487-1488.
28. Kim S, Whitley CB, Jarnes Utz JR. Correlation between urinary GAG and anti-idursulfase ERT neutralizing antibodies during treatment with NICIT immune tolerance regimen: A case report. *Mol Genet Metab.* 2017;122(1-2):92-99.

29. Ngu LH, Ong Peitee W, Leong HY, Chew HB. Case report of treatment experience with idursulfase beta (Hunterase) in an adolescent patient with MPS II. *Mol Genet Metab Rep.* 2017;12:28-32.
30. Nishiyama K, Imai T, Ohkubo K, Sanefuji M, Takada H. Resolution of Hydronephrosis in a Patient With Mucopolysaccharidosis Type II With Enzyme Replacement Therapy. *Urology.* 2017;101:163-165.
31. Gupta A, Uttarilli A, Dalal A, Girisha KM. Hunter syndrome with late age of presentation: clinical description of a case and review of the literature. *BMJ Case Rep.* 2015;2015.
32. Madireddi J, P S, Shetty RK, Prabhu M, K M G. Hunter syndrome with its typical heart: a close mimic to rheumatic heart. *BMJ Case Rep.* 2015;2015.
33. Akiyama R, Murakami Y, Sengoku A, Sonoda K-H. A case of mucopolysaccharidosis (MPS) II diagnosed from the appearance of optic nerve head swelling. *Neuro-Ophthalmology Japan.* 2018;35(1):4.
34. Barth AL, de Magalhães TSPC, Reis ABR, et al. Early hematopoietic stem cell transplantation in a patient with severe mucopolysaccharidosis II: A 7 years follow-up. *Mol Genet Metab Rep.* 2017;12:62-68.
35. Jarstad A, Meeker A, Ko M. Ophthalmic findings in a hunter syndrome patient on enzyme replacement therapy. *Neurology.* 2017;88(16).
36. Moreno LJ, Sanchez-Gomez A, Satizabal JM. Short term impact from enzyme replacement therapy on patients with attenuated Hunter syndrome (MPS II) showing complex heart disease. *Molecular Genetics and Metabolism.* 2017;120(1-2).
37. Bettocchi I, Ortolano R, Baronio F, Bertola F, Pession A, Cassio A. An atypical patient with Hunter syndrome. *Journal of Inherited Metabolic Disease.* 2016;39(S266).
38. Romero FHC, Martinez JIN, Barragan DEC, Escobar IG. Severe adverse reaction to idursulfase in 3 Mexican brothers with MPS-II: Case series. *Allergy: European Journal of Allergy and Clinical Immunology.* 2016;71:1.