

## ULTRA – RARE DISEASE EXAMPLE: SURVIVAL IN PATIENTS WITH NIEMANN PICK-C DISEASE



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### BACKGROUND AND RATIONALE

- Niemann Pick Type-C (NP-C) disease is an **ultra rare condition**
- **Inherited** metabolic disorder characterised by an inability of the body to transport cholesterol and lipids inside of cells.
- Abnormal accumulation of these substances **damages various tissues of the body, including brain tissue.**
- Can be **fatal** within the first few months after birth or chronically progresses and remains undiagnosed well into adulthood.
- Most cases are detected during childhood and progress to cause **life-threatening complications** by the second or third decade of life.

## BACKGROUND AND RATIONALE

Zavesca has been **in clinical use** for the treatment of NP-C in Europe and several other countries for **nearly 10 years**



Allows the assessment of long-term clinical outcomes in a clinical practice



This study represents the first and a very large-scale assessment of the potential benefit of Zavesca treatment on the survival of patients with NP-C



## OBJECTIVES

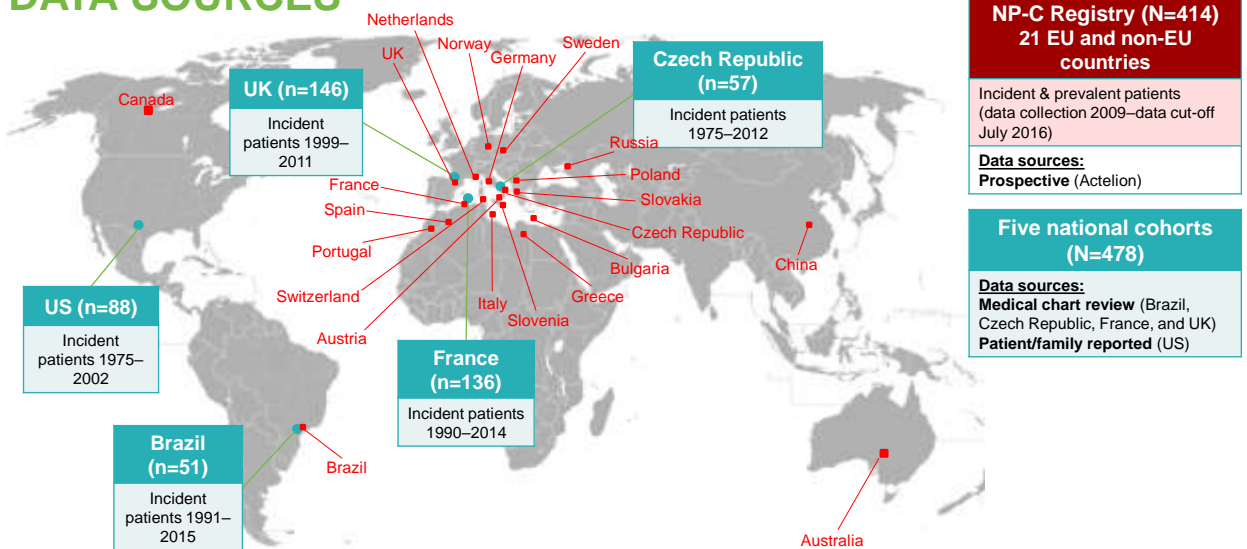
Evaluate **survival** of patients with NP-C from their **NP-C diagnosis**



Assess the effect of **Zavesca treatment** on **survival** rates



## DATA SOURCES



An overall **pool of 789 patients** was defined after removal of duplicate patient data



## DATA AVAILABILITY

For patients where data is available or can be derived

- ▶ Country
- ▶ Gender
- ▶ Date of birth
- ▶ Date of and/or age at diagnosis
- ▶ Date of and/or age at onset of neurological manifestations or at least one symptom (seizures/epilepsy, any coordination deficit [e.g., ataxia, impaired fine motor skills, clumsiness], dysphagia, vertical gaze palsy, dysarthria, cataplexy)
- ▶ Date of and/or age at death; or date of and/or age at last follow-up
- ▶ Date of and/or age at earliest Zavesca start (if applicable)

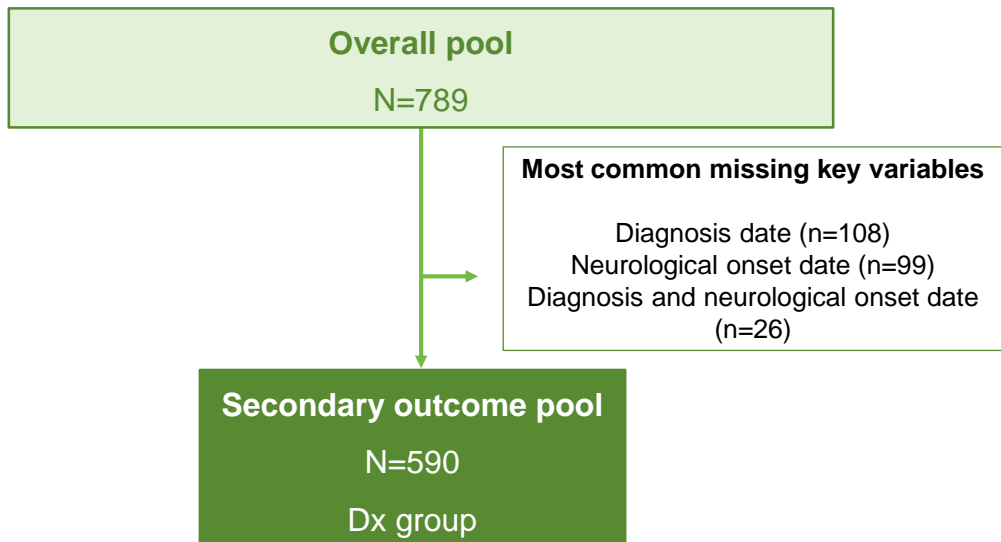


# MANY PATIENTS MISSING KEY VARIABLES

			Missing Key variable				
	Number of patients excluded	Percent	Birth date	Diagnosis Date	Neuro onset date	Death/Censoring	Zavesca start date
COHORTS	1	0.45	x	x	x	x	x
	8	3.62	x	x	x	x	
	1	0.45		x	x	x	x
	1	0.45		x	x	x	
	3	1.36		x	x		
	4	1.81		x			
	1	0.45			x	x	
	56	25.34			x		
6	2.71				x		
8	3.62					x	
REGISTRY	1	0.45	x	x	x		
	2	0.9	x				
	1	0.45		x	x		x
	12	5.43		x	x		
	1	0.45		x		x	
	1	0.45		x			x
	85	38.46		x			
	1	0.45			x		x
26	11.76			x			
1	0.45					x	
1	0.45						

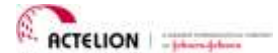
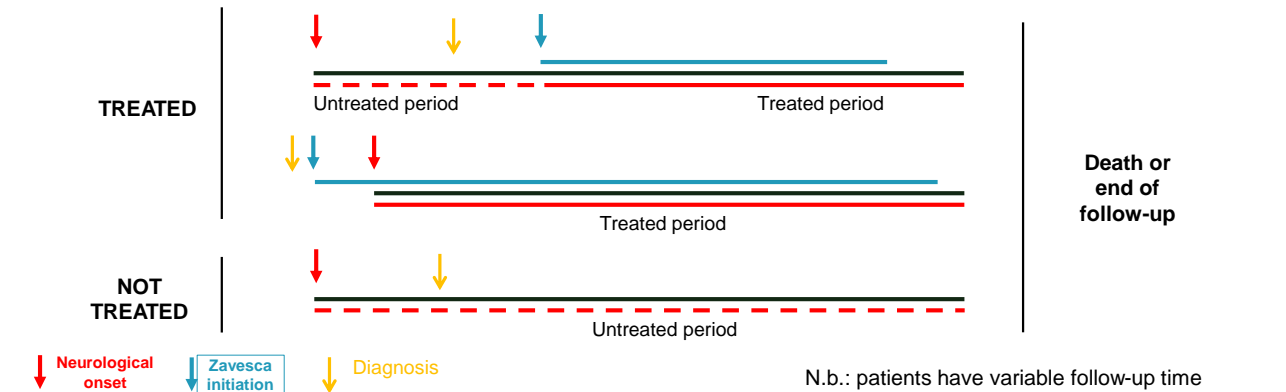


## COHORTS

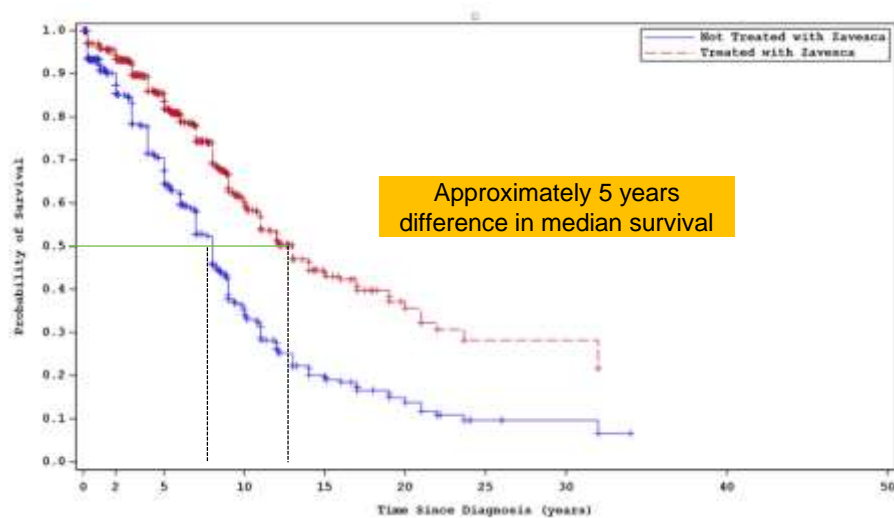


## DELAYED TREATMENT INITIATION

- Patients can have periods when they are not treated (Untreated period) and periods when they are treated with Zavesca (Treated period)
- As soon as a patient has started Zavesca they are considered treated until death or last follow-up



## TIME TO DEATH FROM DIAGNOSIS (N=590)



## CHALLENGES AND LIMITATIONS FOR AN ULTRA RARE CONDITION

- Differential data collection process (recall bias, medical charts vs. patient/family reported, variables collected)
- Quality of data (missing, inconsistent and incomplete)
- Differences in medical practices across countries and eras
- Potential confounding factors that may influence survival, such as Zavesca availability, Zavesca treatment duration, and era of diagnosis
- **Confounders not collected (concomitant treatments, co-morbidities)**

