EE506

RNA Interference Therapies for ATTRv Amyloidosis with Polyneuropathy: Differential Healthcare Resource Use and Direct and Indirect Cost Consequences Associated with Vutrisiran vs Patisiran

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Conclusions

- **Using vutrisiran as an alternative to patisiran in treating hereditary transthyretin (ATTRv) amyloidosis with polyneuropathy has economic advantages in terms of direct healthcare resource use and societal and fiscal impacts**
- **The favorable economic impacts of vutrisiran are attributable to its administration profile (subcutaneous [SC] injection every 3 months [Q3M]), which, when compared with the administration profile of patisiran (intravenous [IV] infusion every 3 weeks [Q3W]), requires less frequent dosing sessions and less time per dosing session, and obviates the need for premedication to minimize the risk of infusion reactions**
- **The economic benefits of vutrisiran relative to patisiran were largely driven by the avoidance of patient work productivity losses associated with treatment; additional benefits were noted in terms of direct healthcare cost savings (due to avoidance of premedication use and decreased treatment administration costs)**
- **The economic benefits of vutrisiran were consistently noted across the seven countries investigated in this analysis**

Background and Rationale

Background

- ATTRv amyloidosis is a rare, underdiagnosed, rapidly progressive, debilitating, and fatal disease caused by variants in the *TTR* gene that result in misfolded transthyretin (TTR) protein accumulating as amyloid deposits in multiple organs and tissues[1–4]
- Vutrisiran and patisiran are approved RNAi therapies that demonstrate comparable efficacy in halting or reversing progression of ATTRv amyloidosis with polyneuropathy, based on the Phase 3, open-label HELIOS-A study[5–8] and the Phase 3, placebo-controlled APOLLO study[9–11], respectively
- Vutrisiran is administered subcutaneously Q3M[7,8] and patisiran intravenously Q3W[10,11]

Objective

- The objective of this analysis is to estimate the differential impacts of vutrisiran and patisiran in terms of healthcare resource use costs, indirect productivity loss costs, and fiscal outcomes in seven countries, to better characterize their relative economic impacts

Methods

- A societal perspective cost comparison analysis was conducted to explore the economic outcomes (in terms of direct healthcare resource use, work productivity, and tax revenue collections) associated with using vutrisiran vs patisiran for the treatment of ATTRv amyloidosis with polyneuropathy
- To estimate economic consequences with respect to healthcare resource use, the analysis considered resources required and associated costs for the administration of each treatment (**Table 1**)
  - Administration of patisiran required premedication (to minimize the risk of infusion reactions) and healthcare provider effort/other resources for IV infusion of each dose; administration of vutrisiran required no premedication and relatively minimal healthcare provider effort/other resources for SC injection of each dose
  - Drug acquisition costs for vutrisiran and patisiran and costs associated with clinical outcomes of treatment were not included as part of this analysis, as it was assumed that both treatments have comparable clinical efficacy and (therefore) parity pricing

Table 1. Direct healthcare costs associated with IV infusion (with premedication) and SC injection

	Premedication cost per IV infusion	IV infusion/SC injection cost per administration		
		IV outpatient	SC outpatient	Source
France	Included in admin cost	€650.11	€650.11	[12]
Germany	€12.96	€50.91	€4.66	[13]
UK	£9.91	£470.81	£90.49	[14]
Italy	€2.86	€9.71	€6.97	[15]
Spain	€1.65	€249.90	€249.90	[16]
Portugal	€3.80	€20.20	€3.70	[17]
Sweden	SEK 34.99	SEK 6,037.00	SEK 3,076.00	[18]

- Work productivity impacts were estimated based on modeling of patients' short-term work absences associated with the dosing schedules and administration routes of vutrisiran and patisiran (**Table 2**, **Table 3**)
  - Estimates of time lost from work with each treatment were obtained and then adjusted to account for age-specific employment rates in the general population at the average age of a patient in HELIOS-A; the estimates resulting from this adjustment were, in turn, further adjusted to reflect the reduced employment rates of patients with ATTRv amyloidosis, compared with the general population, as observed in clinical trials of vutrisiran[5]
  - For each country in the analysis, adjusted estimates of time lost from work with vutrisiran and patisiran were then monetized by applying age-specific, country-specific wage rates to these estimates
- To estimate likely tax revenue impacts (reflecting fiscal burden to the government) resulting from work productivity impacts of a given treatment, we applied the tax wedge rate for each country to the monetary value of lost work productivity (estimated as described previously) for that country
  - The tax wedge rate is defined as the national average percentage difference between the net take-home pay of an employee and the gross labor cost paid per employee by the employer (accounting for net individual and company contributions to income taxes and social benefits)
  - Country-specific tax wedges ranged from 27.2% to 39.2% (sourced from the OECD[19]); employment activity rates and age-specific wages were sourced from the OECD and various national statistics sources[20–29]
- Results were reported as cost per 100 persons treated (over a 10-year time horizon) with either treatment option for each of the seven countries included in the analysis

Table 2. Work loss per treatment administration for employed patients

Product and dose	Travel time to, and wait time in, healthcare facility	Treatment administration time	Work loss per administration[a]
Vutrisiran 25 mg	2 hours	< 5 mins	2 hours
Patisiran 0.3 mg/kg	2 hours	3.5 hours	5.5 hours

The travel and wait time for treatment administration has been standardized in this analysis, though these estimates may vary by country.
[a]Work loss per administration comprises travel time, wait time, and treatment administration time.

Table 3. Work loss per year for employed patients

Product and dose	Frequency	Administrations per year	Annual work loss (work loss per administration × administrations per year)
Vutrisiran 25 mg	Every 3 months	4.0	8 hours
Patisiran 0.3 mg/kg	Every 3 weeks	17.4	95.7 hours

Results

Healthcare resource utilization costs and work productivity and tax revenue impacts

Table 4 and **Table 5** summarize the direct costs of healthcare resource use, the indirect costs from work productivity loss, and the total tax revenue loss per 100 patients (over a 10-year time horizon) treated with vutrisiran and patisiran, respectively

Table 4. Direct healthcare resource use costs, work productivity loss costs, and tax revenue loss associated with vutrisiran (per 100 patients treated over a 10-year time horizon)

Country	Healthcare resource utilization costs		Work productivity loss		Fiscal loss
	Administration (€)	Premedication (€)	Time lost (hours)	Cost of time lost (€)	Tax revenue loss (€)
UK[a]	148,886	0	2,214	27,517	8,365
France	89,561	0	1,895	29,452	11,545
Germany	17,165	0	1,741	49,245	16,202
Italy	25,673	0	1,749	23,031	8,038
Portugal	143,735	0	1,803	13,950	4,408
Spain	917,897	0	1,661	22,079	7,595
Sweden[b]	951,725	0	2,189	41,592	15,597

[a]Exchange rate, 1.17 EUR/GBP. Source: October 5, 2023, oanada.com. [b]Exchange rate, 0.084 EUR/SEK. Source: October 5, 2023, oanada.com.

Table 5. Direct healthcare resource use costs, work productivity loss costs, and tax revenue loss associated with patisiran (per 100 patients treated over a 10-year time horizon)

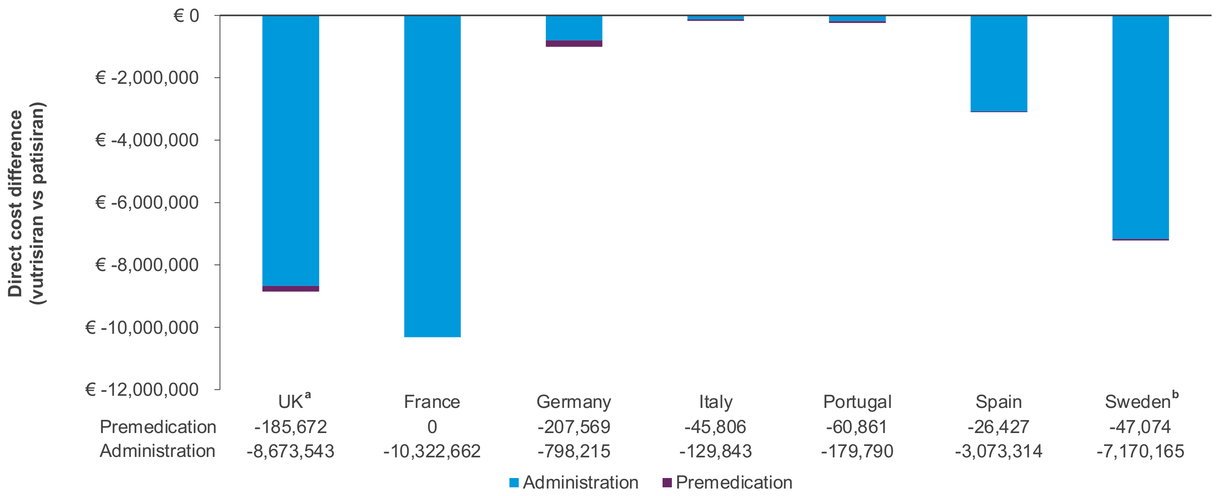
Country	Healthcare resource utilization costs		Work productivity loss		Fiscal loss
	Administration (€)	Premedication (€)	Time lost (hours)	Cost of time lost (€)	Tax revenue loss (€)
UK[a]	8,822,429	185,672	26,480	329,038	100,028
France	10,412,223	0	22,660	352,176	138,053
Germany	815,379	207,569	20,812	588,851	193,732
Italy	155,516	45,806	20,914	275,400	96,115
Portugal	323,525	60,861	21,559	166,813	52,713
Spain	3,991,211	26,427	19,865	264,011	90,820
Sweden[b]	8,121,890	47,074	26,172	497,337	186,501

[a]Exchange rate, 1.17 EUR/GBP. Source: October 5, 2023, oanada.com. [b]Exchange rate, 0.084 EUR/SEK. Source: October 5, 2023, oanada.com.

Avoided healthcare resource utilization costs and productivity loss with vutrisiran vs patisiran

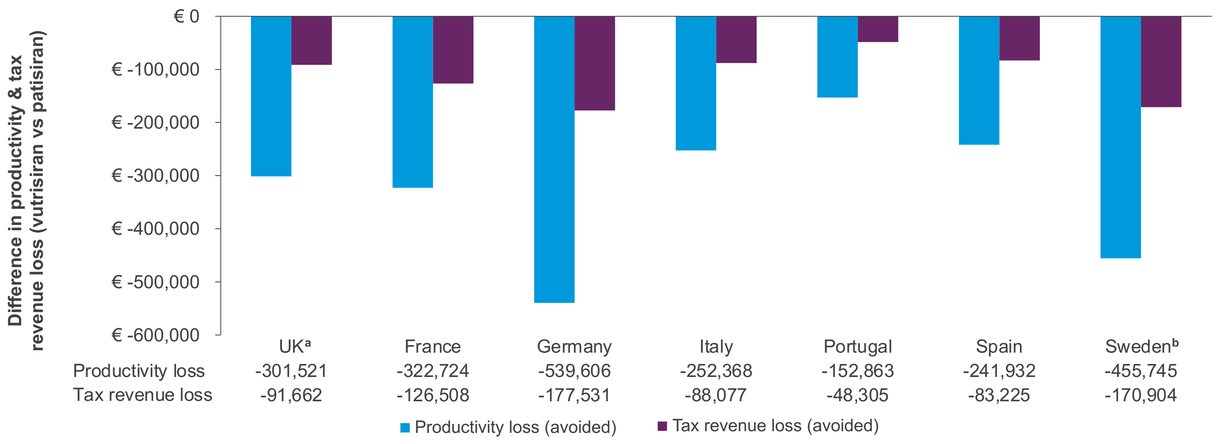
- **Figure 1** summarizes the difference between vutrisiran and patisiran in terms of direct healthcare resource use costs, while **Figure 2** summarizes the difference between vutrisiran and patisiran in terms of work productivity loss costs and tax revenue loss
  - Compared with patisiran, vutrisiran results in direct healthcare resource use cost savings and averts productivity and tax revenue losses

Figure 1. Direct healthcare resource use costs avoided with vutrisiran vs patisiran (per 100 treated patients over a 10-year time horizon)



[a]Exchange rate, 1.17 EUR/GBP. Source: October 5, 2023, oanada.com. [b]Exchange rate, 0.084 EUR/SEK. Source: October 5, 2023, oanada.com.

Figure 2. Work productivity loss costs and tax revenue loss avoided with vutrisiran vs patisiran (per 100 treated patients over a 10-year time horizon)



[a]Exchange rate, 1.17 EUR/GBP. Source: October 5, 2023, oanada.com. [b]Exchange rate, 0.084 EUR/SEK. Source: October 5, 2023, oanada.com.

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Abbreviations: ATTRv, hereditary transthyretin (v for variant); IV, intravenous; Q3M, every 3 months; Q3W, every 3 weeks; RNAi, RNA interference; SC, subcutaneous.
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