A Cost-Effectiveness Comparison of Icatibant and C1-Esterase Inhibitor Concentrate for the Symptomatic Treatment of Acute Attacks of Types I and II Hereditary Angioedema in the UK Setting

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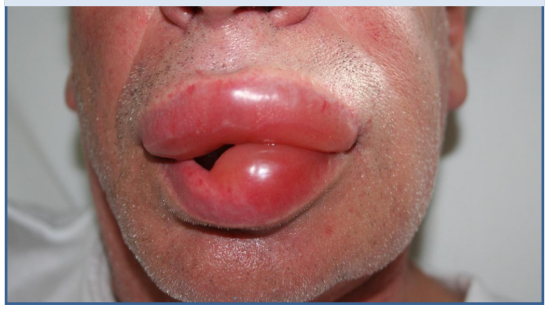
PSY27

OBJECTIVES

- Hereditary angioedema (HAE) type I and II are bradykinin-mediated swellings of the skin and mucosal tissues characterised by debilitating, painful and potentially life-threatening acute attacks lasting 2–5 days (Figure 1).[1–3]
- HAE type I and II are linked to genetic defects in the SERPING1 gene, leading to a deficiency of C1-esterase inhibitor (C1-INH) protein.[4]
- As both bradykinin and C1-INH are involved in the pathogesis of HAE, treatment options for HAE attacks include the bradykinin antagonist icatibant (Firazyr®, Shire HGT Inc.) and C1-INH inhibitors (e.g. Berinert®, CSL Behring).
- The efficacy and safety of these treatments were demonstrated in several Phase III randomised controlled trials.[5–7] However, these assessments were made using different clinical endpoints and, to date, no head-to-head studies have been conducted that directly compare these two HAE treatments.
- There is also a lack of comparative cost-effectiveness data between the two treatments. In the absence of such data, a cost-effectiveness model was performed to compare icatibant and C1-INH (CSL Behring) 20 IU/kg in a UK clinical perspective setting. The results are presented here.
- This is the first comparative health economic model presented for HAE.

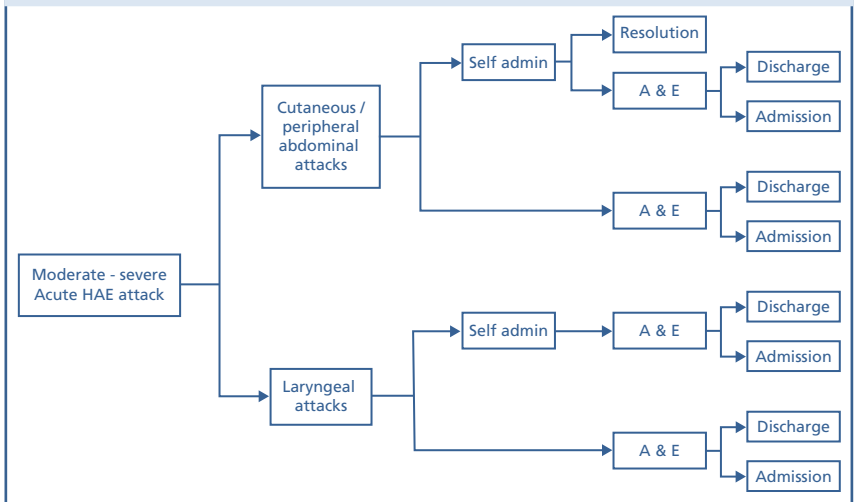
Figure 1. Image of a patient with HAE symptoms



METHODS

- A probabilistic cost-utility model was constructed in Microsoft Excel to estimate the cost-effectiveness of icatibant (30 mg *subcutaneous*) and C1-INH (Berinert®, CSL Behring) (20 IU/kg *intravenous*) in the UK setting, using data from Scotland and Wales (Figure 2).
- An indirect comparison of three icatibant studies (**F**or **A**ngioedema **S**ubcutaneous **T**reatment [FAST]-1, -2 and -3)[5,6] and one C1-INH (CSL Behring) study (**I**nternational **M**ulti-center **P**rospective **A**ngioedema **C**1-Inhibitor **T**rial [I.M.P.A.C.T]-1)[7] was undertaken to compare treatment efficacy (Poster PSY10).
- These indirect comparison data were input into the model along with the following costs: drug cost; administration, monitoring and supportive care (taken from NHS reference costs 2009–2010); method and location of administration; number of attacks per year (to include the cost of vaccination and self-administration training); and requirement of hepatitis A and B vaccinations. These variables comprised the base-case scenario.
- Sensitivity analyses were performed to discover whether variations in any of the above values significantly impacted the cost-effectiveness comparisons.
- Quality-adjusted life years (QALYs) were estimated by combining data for the time-to-onset of symptom relief (the primary endpoint of the majority of relevant trials) and utility weights for two health states: during an attack (the period of time before the onset of symptom relief), and following recovery from the attack (after onset of symptom relief).
  - Time-to-onset of symptom relief for icatibant-treated patients was estimated using a survival function and applying hazard ratios from the indirect comparison (Poster PSY10).
- A systematic review was performed to identify health-state utility value estimates relevant to the analysis. Two sources of data were identified (both unpublished):
  - An Expert Panel scored quality-of-life for moderate and severe HAE attacks using the EQ-5D.
  - Utility weights were estimated from visual analogue scale (VAS) scores observed in the FAST trials.
- In the cost-utility model, QALYs were estimated over the model time frame of 96 h (a duration that was estimated to include 99.9% of all moderate-to-severe attacks).

Figure 2. Administration and monitoring algorithm



Self-administration and administration in a hospital setting are modelled as shown in the model structure diagram above. Patients with cutaneous/peripheral/abdominal attacks may self-administer therapy or receive treatment in hospital. Following self-administration, the patient's symptoms may resolve and require no further care, or they may attend accident and emergency (A&E) for additional supportive care, treatment, and/or monitoring in hospital. Patients whose symptoms resolve during their A&E attendance are discharged; patients whose symptoms do not resolve may be admitted for further supportive care, treatment, and/or monitoring. Patients with laryngeal attacks may receive initial self-administered treatment or receive treatment in hospital. All patients with laryngeal attacks will proceed to hospital for monitoring and possibly, additional treatment.

RESULTS

Cost-effectiveness

- In the base-case analysis, the total costs per attack were estimated as £1,577 for icatibant and £2,169 for C1-INH (CSL Behring) 20 IU/kg (Figure 3).
- This is equivalent to a saving of £592 (95% CI; £349–£715) per attack with icatibant (Table 1).
- The sensitivity analyses that affected these model results were:

In favour of icatibant
- Increasing patient weight
- Increasing proportion of patients who self-administer icatibant
- Lower incidence of repeat icatibant dosing (at least 65% of patients using one icatibant syringe per attack)

In favour of C1-INH (CSL Behring)
- C1-INH (CSL Behring) dose <20 IU/kg
- Higher incidence of repeat icatibant dosing (fewer than 64% of patients using one icatibant syringe per attack)

QALYs

- The economic analysis demonstrated that the difference in QALYs between treatments was very small, and therefore not significant (Table 1).
- This difference was equivalent to approximately 0.75 quality-adjusted life hours, in favour of icatibant.

Figure 3. Estimated cost per attack of icatibant and C1-INH (CSL Behring)

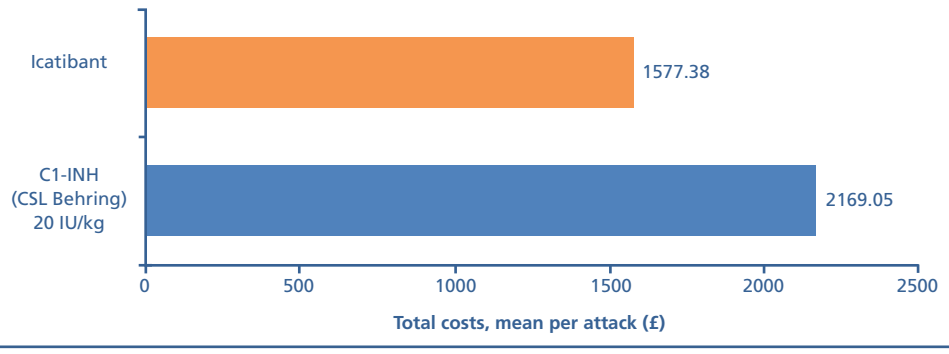


Table 1. Comparison of estimated and incremental costs per attack and incremental outcomes per attack of icatibant 30 mg *subcutaneous* and C1-INH (CSL Behring) 20 IU/kg *intravenous*.

Estimated costs (mean per attack, £)[†]	Icatibant	C1-INH (CSL Behring) 20 IU/kg
Drug	1546.20	1954.62
Administration, monitoring and supportive care	31.03	211.70
Vaccination	0.00	0.39
Self-administration training	0.15	2.35
Total costs (mean per attack, £)	***1577.38***	***2169.05***
PSA[‡] 95% CI	*1504–1679*	*1987–2266*
Incremental costs (mean per attack, £)	***Icatibant vs C1-INH (CSL Behring) 20 IU/kg***	
Drug	-408.41	
Administration	-180.67	
Vaccination	-0.39	
Self-administration	-2.20	
Total (mean per attack, £)	***-591.67***	
Incremental outcomes[§]	***Icatibant vs C1-INH (CSL Behring) 20 IU/kg***	
Mean time with symptoms, h	-2.54	
QALYs	0.0000852	

[†]Utility weight estimates were identical for all comparators. Costs relate to SmPC data only. Patient Access Scheme discounts have not been applied.
[‡]PSA = Probabilistic Sensitivity Analysis.
[§]Incremental outcomes were calculated by subtracting the outcome estimates for the comparator from the outcome estimates for icatibant.

CONCLUSIONS

- **The health economic analyses presented here demonstrate that icatibant reduces costs versus C1-INH (CSL Behring) 20 IU/kg in the treatment of HAE type I and II attacks in the UK setting.**
- **Icatibant reduces total treatment costs, mainly due to lower drug acquisition costs, although savings with administration costs are also expected as a higher proportion of icatibant patients self-administer treatment.**

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Disclosures

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