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Comparison of Healthcare Costs Between Tocilizumab and Conventional Immunosuppressants in Patients With Large-Vessel Vasculitis
A Retrospective Study Using Claims Data in Japan

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Background

- Large-vessel vasculitis (LVV) is an autoimmune inflammatory disease affecting large arteries and includes Takayasu arteritis (TAK) and giant cell arteritis (GCA). Glucocorticoids (GCs) remain the mainstay of treatment, but long-term use is associated with substantial adverse effects, including infections and osteoporosis/fractures [1,2].
- Steroid-sparing therapies include conventional immunosuppressants such as azathioprine (AZA) and methotrexate (MTX), as well as the biologic agent tocilizumab (TCZ), which is often selected for patients with severe disease or those requiring GC dose reduction [1]. TCZ has demonstrated clinical benefit and GC-sparing effects [3,4]; however, its drug cost is substantially higher than that of conventional immunosuppressants (approximately €790 per 4 weeks for TCZ vs €12–30 per month for AZA/MTX in Japan, depending on dose) [5,6]. Therefore, its economic impact should be evaluated in the context of overall healthcare costs, including hospitalization and other medical resource use.
- However, real-world evidence assessing TCZ within the broader healthcare cost profile remains limited.

Objective

To characterize overall healthcare costs and their cost components associated with TCZ treatment in patients with LVV using Japanese claims data, with AZA/MTX as the comparator.

Conclusion

Despite higher drug costs, the lower hospitalization costs observed with TCZ suggest that it may partly reduce the healthcare burden associated with GC-related complications, including infections and osteoporosis/fractures.

Methods

Study Design and Population

- Retrospective cohort study using Medical Data Vision hospital-based claims data from April 2008 to July 2023.
- Eligibility criteria and the study timeline are shown in Fig. 1.
- Patients were classified by index treatment into oral GC + TCZ or oral GC + AZA/MTX groups and followed until their last available claim, regardless of treatment discontinuation, switching, or interruption.
- TAK and GCA were analyzed separately.

Cost Definitions and Outcomes

- Costs were estimated from the public payer perspective, adjusted to 2024 prices, and converted at €1 = ¥163.95. Relevant conditions were identified using ICD-10 codes, and costs were categorized as medication, examination, surgery/intervention, and hospitalization. Hospitalization periods were identified from discharge summaries, and hospitalization costs were calculated from medical procedure claims.
- Disease-related costs included costs associated with LVV and cardiovascular/cerebrovascular diseases.
- Comprehensive disease-related costs (CDRC) additionally included infection- and osteoporosis/fracture-related costs.
- The primary outcome was mean CDRC per 30 days during follow-up. Secondary outcomes included disease-related costs, cost components, 360-day cost trends, hospitalization, surgery, and GC use.

Statistical Analysis

- For each patient, 30-day mean CDRC was calculated as total CDRC / follow-up days × 30 and compared using a generalized linear model with a gamma distribution and log link. Adjusted cost ratios (aCRs) with 95% confidence intervals were estimated.
- Models were adjusted for age, sex, maximum daily PSL-equivalent dose during the 90-day pre-index period, and comorbidities, hospitalization days, and outpatient visits during the preceding 3 months. Disease-related costs were analyzed similarly.
- Cost components and longitudinal trends were summarized using unadjusted means; other outcomes were described as n (%) or median [IQR].

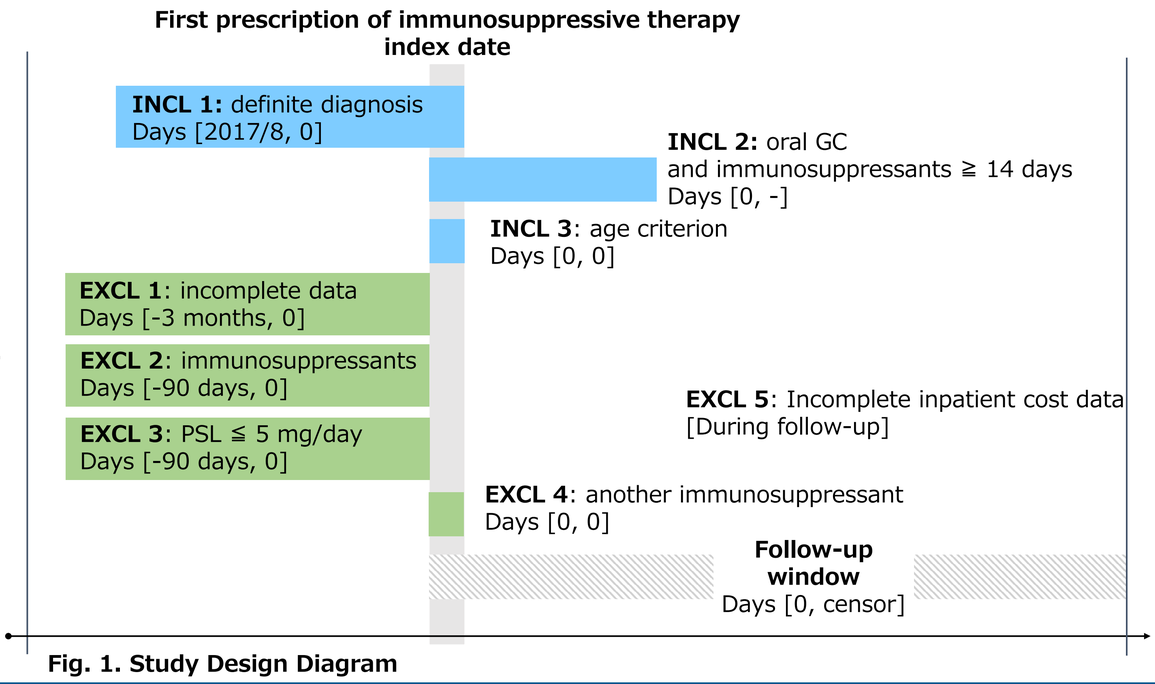


Fig. 1. Study Design Diagram

Results

Fig. 2. Patient Flowchart

Patients diagnosed with TAK or GCA between August 2017 and July 2022
TAK Patients: N=4,275
GCA Patients: N=3,221

Inclusion criteria
- Oral GC or immunosuppressant use for ≥14 days after diagnosis
- Age at index: TAK ≥18 years; GCA ≥50 years

Exclusion criteria
- <3 months of baseline data
- Immunosuppressant use within 3 months before index
- Minimum oral GC dose ≤5 mg/day within 90 days before index
- Index treatment other than TCZ/AZA/MTX or concomitant initiation of ≥2 agents
- Missing claims required for inpatient cost calculation

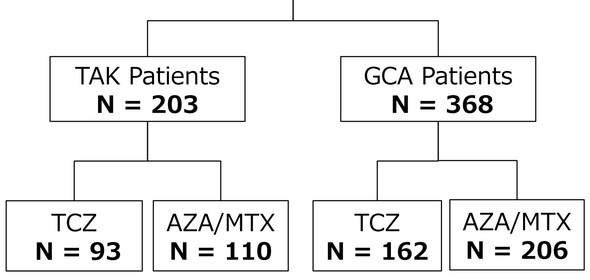


Table 1. Baseline Characteristics

	TAK Patients		GCA Patients	
	TCZ (N=93)	AZA/MTX (N=110)	TCZ (N=162)	AZA/MTX (N=206)
Female	75 (80.6)	75 (68.2)	109 (67.3)	109 (52.9)
Age	37.0 [25.0–56.0]	57.0 [33.0–68.0]	76.0 [71.0–80.0]	74.5 [69.0–80.0]
Comorbid conditions within 3 months before the index				
Cerebral /Cardiovascular disease	2 (2.2)	4 (3.6)	2 (1.2)	4 (1.9)
Infection	4 (4.3)	2 (1.8)	8 (4.9)	6 (2.9)
Diverticulitis /Perforation	0	1 (0.9)	0	0
Liver dysfunction	7 (7.5)	15 (13.6)	17 (10.5)	22 (10.7)
Renal dysfunction	6 (6.5)	6 (5.5)	10 (6.2)	10 (4.9)
Malignant tumor	6 (6.5)	15 (13.6)	31 (19.1)	42 (20.4)
Glucocorticoid use within 90 days before the index				
Maximum daily prednisolone equivalent dose (mg/day)	12.0 [10.0–19.0]	12.5 [9.0–17.5]	20.0 [10.0–35.0]	11.0 [8.0–17.5]
Visit frequency within 3 months before the index				
Number of outpatient visits	3.5 [2.0–6.0]	3.0 [2.0–4.0]	3.0 [2.0–6.0]	3.0 [2.0–5.0]
Number of inpatient days	0 [0–7.0]	0 [0–8.0]	3.0 [0–15.0]	0 [0–12.0]

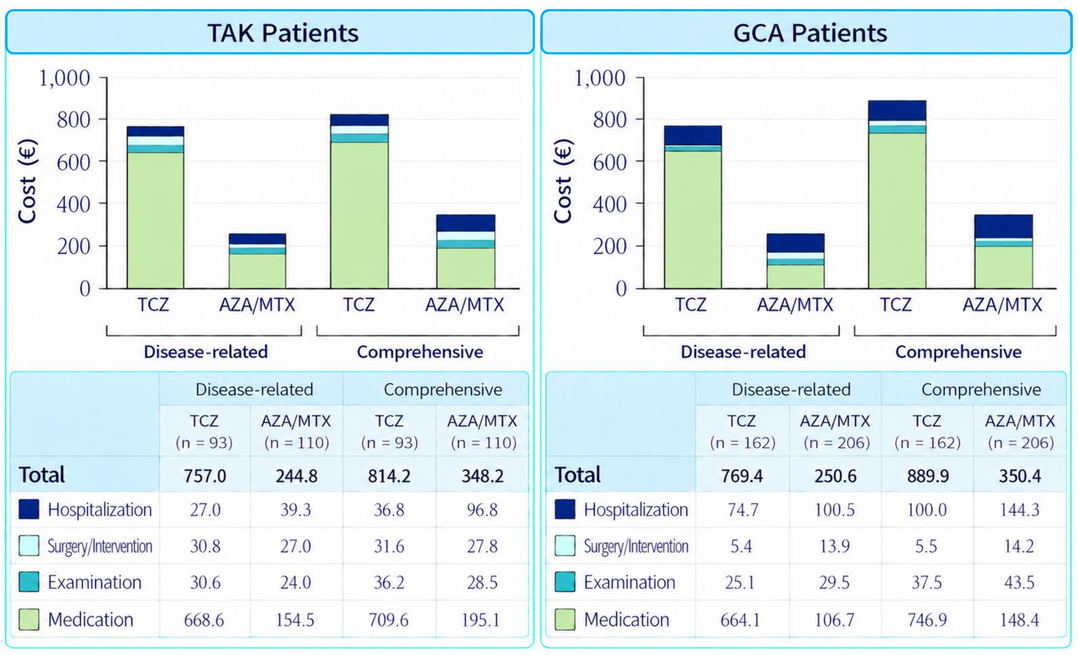
Values are presented as n (%) or median [IQR]

Table 2. Adjusted 30-Day Mean Cost Ratios (aCRs)

	TAK Patients	GCA Patients
Disease-related cost ratio	**3.09 (2.31-4.13)**	**3.46 (2.70-4.43)**
Comprehensive disease-related cost ratio	**2.66 (2.02-3.51)**	**3.02 (2.41-3.79)**

Values are presented as aCRs (95% CIs), with the AZA/MTX group as the reference.

Fig. 3. Unadjusted Mean 30-Day Healthcare Costs

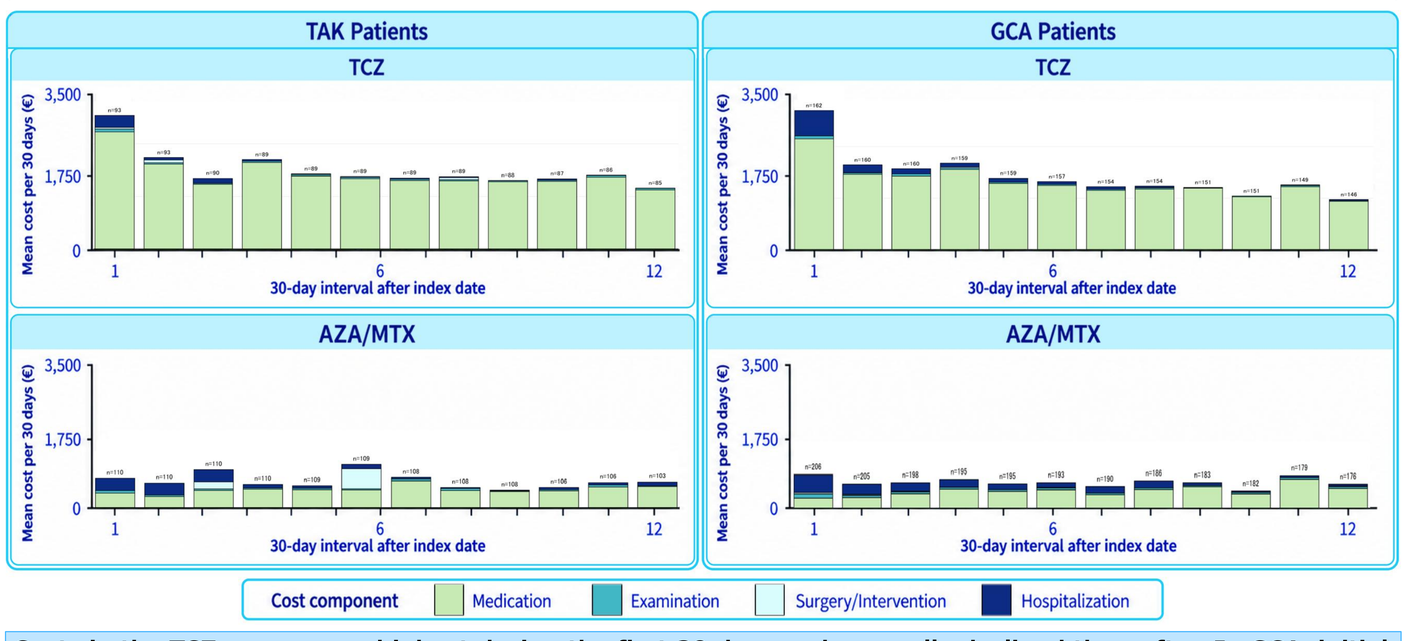


TAK Patients	Disease-related		Comprehensive	
	TCZ (n = 93)	AZA/MTX (n = 110)	TCZ (n = 93)	AZA/MTX (n = 110)
Total	**757.0**	**244.8**	**814.2**	**348.2**
Hospitalization	27.0	39.3	36.8	96.8
Surgery/Intervention	30.8	27.0	31.6	27.8
Examination	30.6	24.0	36.2	28.5
Medication	668.6	154.5	709.6	195.1

GCA Patients	Disease-related		Comprehensive	
	TCZ (n = 162)	AZA/MTX (n = 206)	TCZ (n = 162)	AZA/MTX (n = 206)
Total	**769.4**	**250.6**	**889.9**	**350.4**
Hospitalization	74.7	100.5	100.0	144.3
Surgery/Intervention	5.4	13.9	5.5	14.2
Examination	25.1	29.5	37.5	43.5
Medication	664.1	106.7	746.9	148.4

In both diseases, costs were higher in the TCZ group under both cost definitions, mainly due to medication, whereas hospitalization costs were lower.

Fig. 4. Comprehensive Disease-Related Costs at 30-Day Intervals Over 360 Days



Costs in the TCZ group were highest during the first 30 days and generally declined thereafter. In GCA, initial unadjusted hospitalization costs were higher in the TCZ group.

Table 3. Clinical Events and Glucocorticoid Use During Follow-up

	TAK Patients		GCA Patients	
	TCZ (N=93)	AZA/MTX (N=110)	TCZ (N=162)	AZA/MTX (N=206)
Hospitalization during follow-up				
Comprehensive disease-related hospitalization	31 (33.3)	31 (28.2)	73 (45.1)	70 (34.0)
Comprehensive disease-related hospitalization days*	14.0 [9.0-22.0]	24.0 [8.0-67.0]	17.0 [8.0-38.0]	17.0 [8.0-32.0]
Disease-related hospitalization	29 (31.2)	26 (23.6)	69 (42.6)	52 (25.2)
Disease-related hospitalization days*	12.0 [8.0-17.0]	18.0 [8.0-39.0]	16.0 [8.0-33.0]	14.5 [7.5-28.0]
Surgery during follow-up				
Comprehensive disease-related surgery	9 (9.7)	7 (6.4)	6 (3.7)	9 (4.4)
Fracture-related surgery	1 (1.1)	3 (2.7)	2 (1.2)	3 (1.5)
Disease-related surgery/intervention	8 (8.6)	4 (3.6)	5 (3.1)	7 (3.4)
Glucocorticoid use during follow-up				
Maximum daily PSL-equivalent dose (mg/day)	16.7 [11.0-40.0]	15.5 [10.0-30.0]	29.5 [14.0-52.5]	15.0 [10.0-30.0]
Average daily PSL-equivalent dose (mg/day)	6.4 [3.2-9.4]	6.7 [4.6-9.8]	5.5 [3.3-9.1]	6.9 [4.0-9.2]

Values are presented as n (%) or median [IQR]. *Among hospitalized patients.

The TCZ group had higher comprehensive disease-related hospitalization proportions in both diseases but shorter stays in TAK. Maximum PSL-equivalent doses were higher, whereas average daily doses were lower.

Discussion

1. Despite higher medication costs in the TCZ group (Fig. 3), including infection- and osteoporosis/fracture-related costs reduced the between-group adjusted cost ratios (Table 2). This suggests that complication-related costs may have contributed relatively more to overall healthcare costs in the AZA/MTX group.
2. Regarding longitudinal cost trends, higher pre-index maximum PSL doses and hospitalization days in the GCA TCZ group (Table 1) suggest that greater baseline treatment needs may have contributed to higher initial hospitalization costs. Subsequent cost stabilization may reflect reduced healthcare resource utilization following the initial treatment period (Fig. 4).
3. The higher hospitalization proportion but lower hospitalization costs in the TCZ group (Table 3, Fig. 3) may reflect differences in admission indications and healthcare resource utilization. Admissions for disease assessment or treatment adjustment may have been more common in the TCZ group, whereas infections or fractures may have contributed more to hospitalization burden in the AZA/MTX group. In TAK, shorter comprehensive disease-related hospitalization duration (Table 3) may also have contributed to lower hospitalization costs.
4. Lower average daily GC exposure in the TCZ group (Table 3) may have contributed to a reduced healthcare burden associated with infections and osteoporosis/fractures [2].

Limitations: Residual confounding due to baseline differences and unmeasured disease activity or severity cannot be excluded. The database did not capture healthcare costs incurred at other institutions, potentially underestimating total healthcare costs. Furthermore, patients were classified by index treatment and followed regardless of treatment discontinuation or switching; therefore, estimated costs may not reflect costs incurred during actual treatment exposure.

References

[1] Isobe M, et al. *Circ J.* 2020;84:299–359. [2] Best JH, et al. *Clinicoecon Outcomes Res.* 2019;11:799–807. [3] Stone JH, et al. *N Engl J Med.* 2017;377:317–328. [4] Nakaoka Y, et al. *Ann Rheum Dis.* 2018;77:348–354. [5] Chugai Pharmaceutical. ACTEMRA package insert. 2026. [6] Ministry of Health, Labour and Welfare, Japan. NHI Drug Price Standard, FY2024.

Acknowledgment

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