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Single Day Event

Leveraging Kaplan-Meier and Sankey Diagrams in Real-World Evidence Studies for Enhancing Healthcare Decision-making

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Agenda

- **Real World Evidence**
- **Key Visualization Techniques in RWE**
- **Case study I:** Treatment management for BRAF-mutant melanoma patients with tumor recurrence on adjuvant therapy
- **Case study II:** Real-world treatment patterns in patients with psoriasis taking systemic oral or biologic therapies
- **Conclusion**
- **References**

Real World Evidence

Real-world data (RWD) are data related to patient health status and health care routine.
Sources:

- Electronic Health Records (EHRs)
- Insurance Claims
- Registries

Real-world evidence refers to the clinical evidence on benefits or risks of medical product derived from RWD

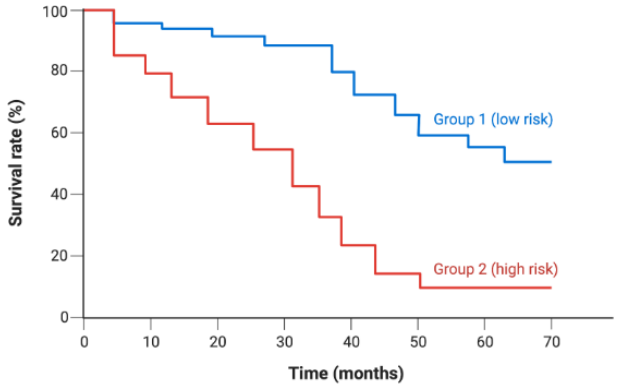
FDA has accepted the use of RWD to generate RWE to support regulatory decisions

Key Visualization Techniques in RWE

Visualization methods help interpret complex information and drive decision-making.

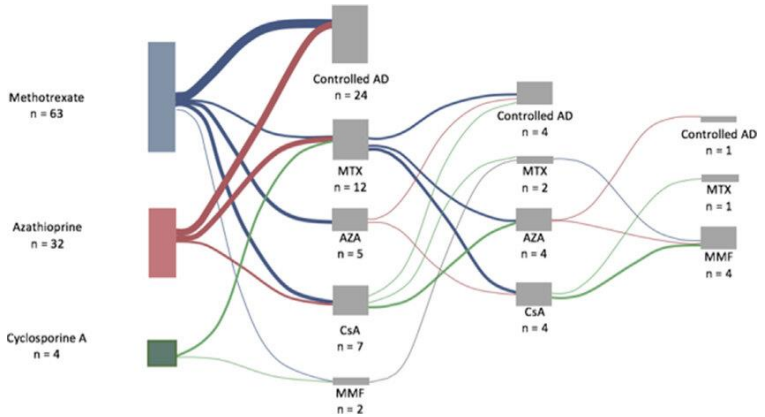
Kaplan-Meier (KM) Curves - Time-to-Event Analysis

- Non-parametric statistical method used to estimate probability of an event over time
- Used in clinical research to assess patient survival rates and visualize outcomes differences between cohorts



Sankey Diagrams – Flow Diagrams of Treatment Journey

- Highlights patient treatment journey
- Helps track therapy changes, medication adherence, and disease progression



Case study I: Treatment management for *BRAF*-mutant melanoma patients with tumor recurrence on adjuvant therapy

Background

- Adjuvant therapy with immune-checkpoint inhibitors (CPI) or BRAF/MEK-directed targeted therapy (TT) improves recurrence-free survival (RFS) for advanced BRAFV600-mutant resected melanoma patients
- Lack of evidences to support which regimen, either anti-PD1 or TT in the adjuvant setting is most effective in preventing recurrence and compare subsequent treatments following tumor recurrence upon upfront adjuvant therapy for treatment management upon DM

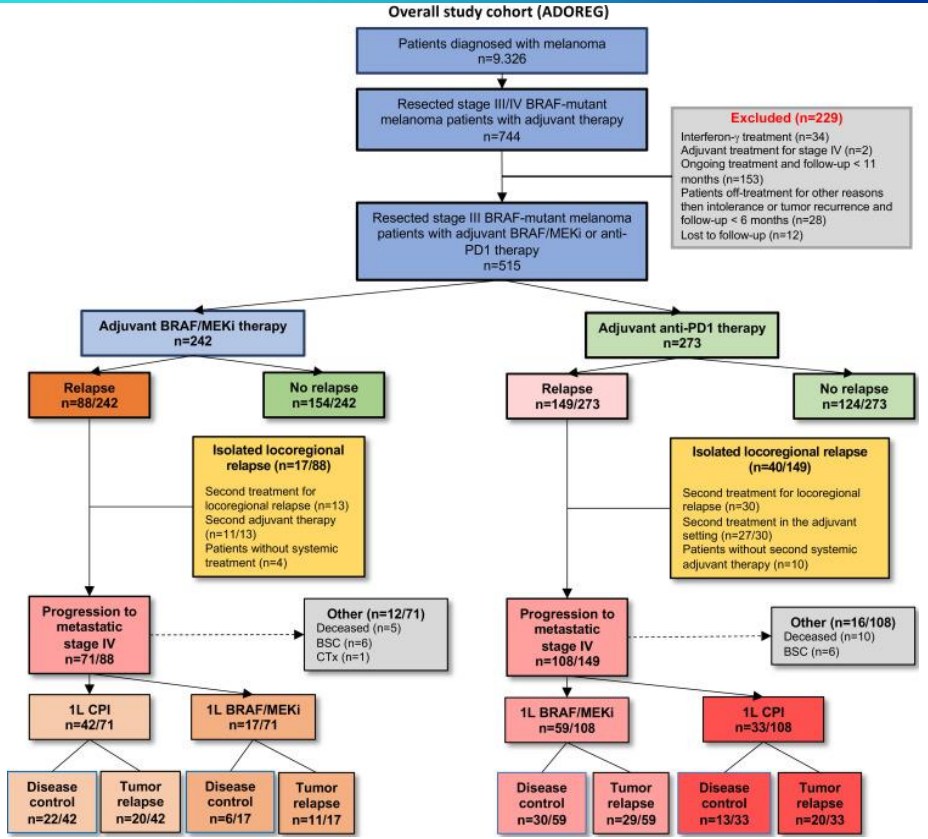
Database

- Real-world skin cancer registry ADOReg of the German Dermatologic Cooperative Oncology Group

Outcomes

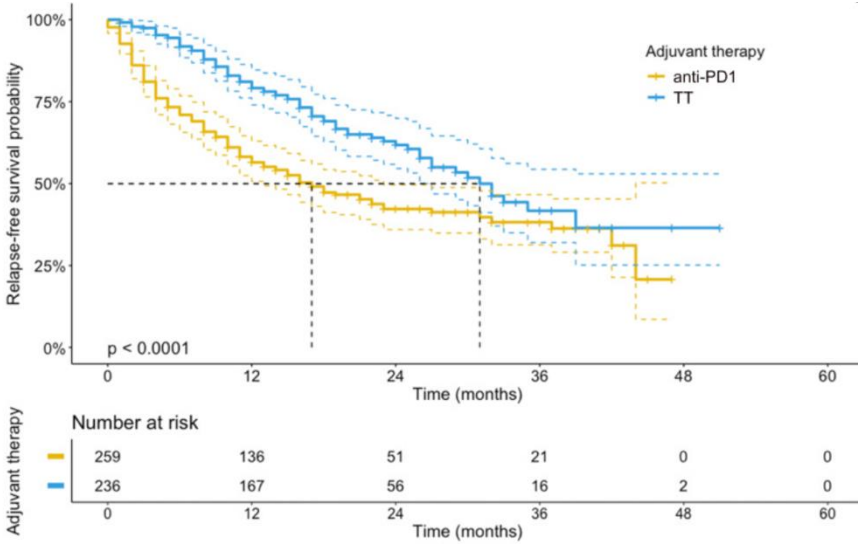
- Primary outcomes included evaluating progression free survival (PFS) following DM and tumor response for 1L therapy for metastatic stage IV post adjuvant failure
- Secondary outcomes included RFS, second RFS and OS

Reference paper

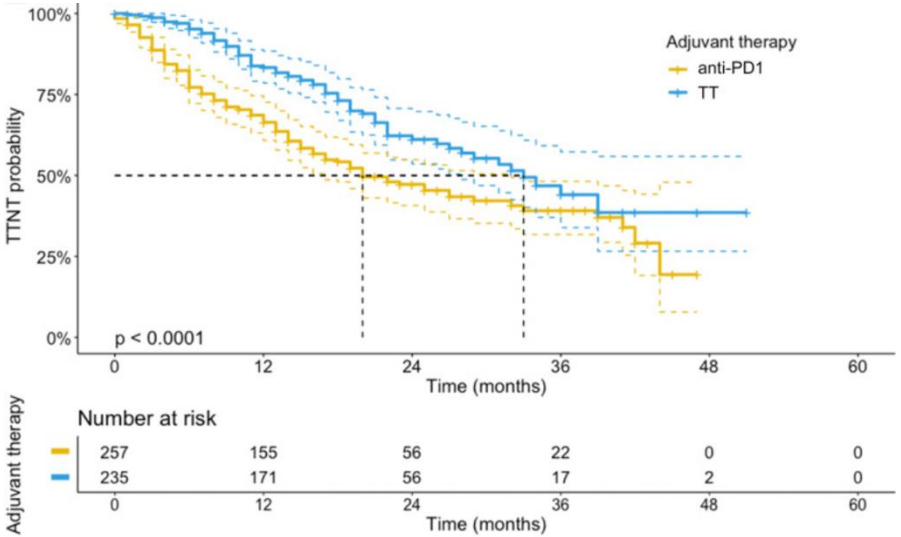


Case study I: Treatment management for *BRAF*-mutant melanoma patients with tumor recurrence on adjuvant therapy

BRAF-mutant stage III melanoma patients treated outside of clinical trials



Median RFS
TT: 31.0 months, 95% CI 26.0 to 36.0
anti-PD1: 17.0 months, 95% CI 11.9 to 22.1



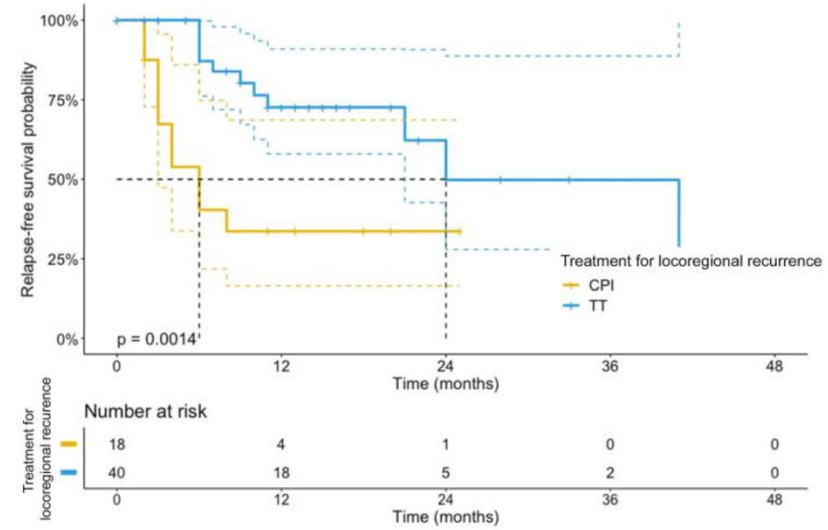
Median TTNT
TT: 33.0, 95% CI 26.6 to 39.4
anti-PD1: 20.0 months, 95% CI 14.3 to 25.7

Reference paper

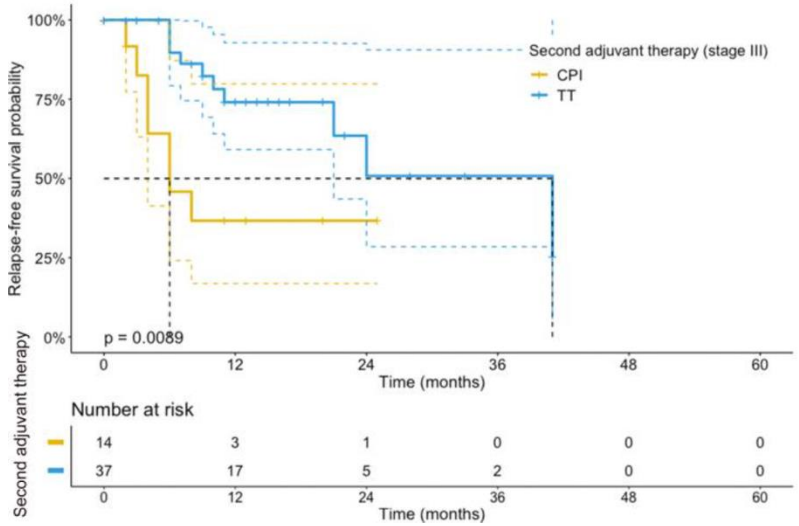
Case study I: Treatment management for *BRAF*-mutant melanoma patients with tumor recurrence on adjuvant therapy

Treatment management for patients with locoregional tumor recurrence

76 patients with locoregional recurrence; 58 patients with treatment for locoregional recurrence; 51 patients with resected locoregional recurrence and subsequent second-line adjuvant treatments.



Median RFS2
TT: 24.0 months; CPI: 6.0 months

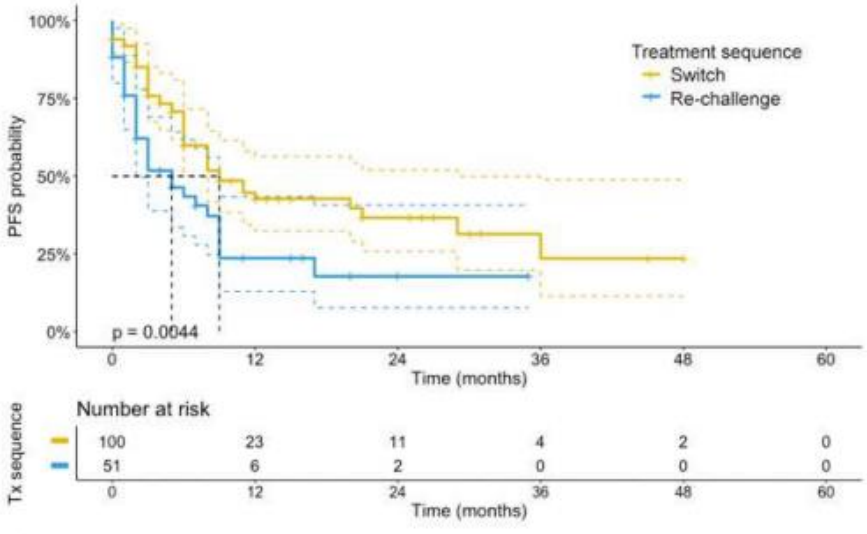


Median RFS2
TT:41.0 months; CPI: 6.0 months

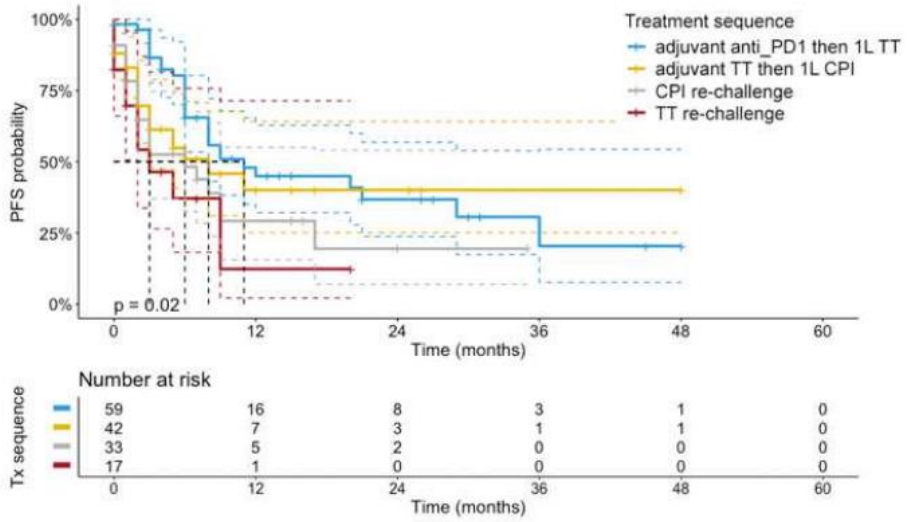
Reference paper

Case study I: Treatment management for *BRAF*-mutant melanoma patients with tumor recurrence on adjuvant therapy

Comparing outcomes between adjuvant therapy and first-line treatment for metastatic stage IV



Median PFS
Switch: 9 months, 95% CI: 5.2-12.8
Re-challenge: 5 months, 95% CI: 1.3-8.7



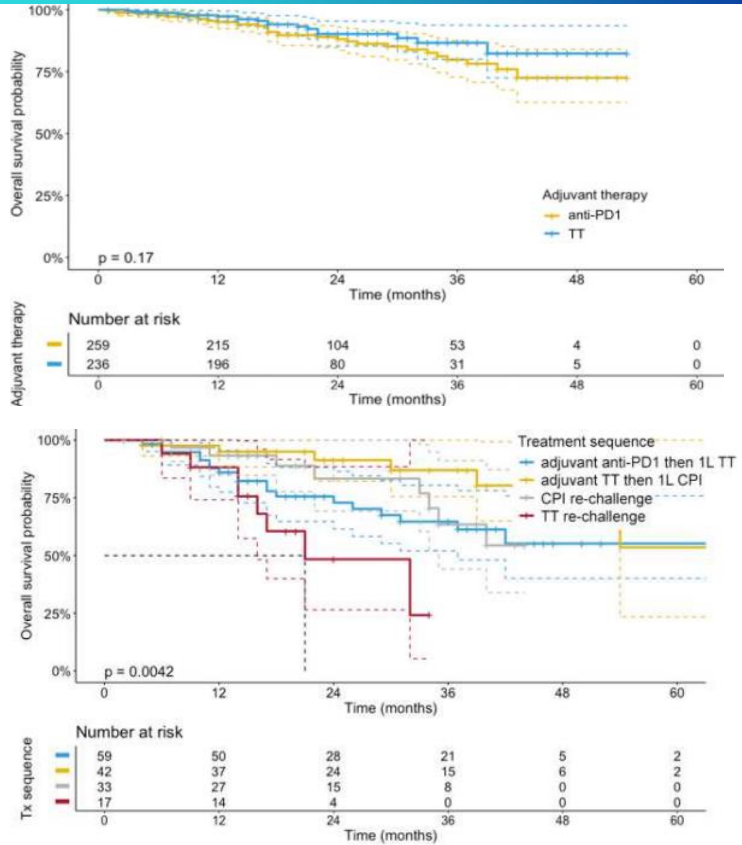
Median PFS
Adj. CPI failure to TT: 11.0 months
Adj. TT failure to CPI: 8.0 months
Adj. TT failure to TT: 3.0 months
Adj. CPI failure to CPI: 6.0 months

Reference paper

Case study I: Treatment management for *BRAF*-mutant melanoma patients with tumor recurrence on adjuvant therapy

- Adjuvant targeted therapy (TT) resulted in a significant reduction of the risk of tumor recurrence compared with adjuvant anti-PD1 treatment
- Despite the significant prolongation of RFS for adjuvant TT patients, OS did not significantly differ between both the adjuvant cohorts
- Patients with resected locoregional recurrence benefit from a second adjuvant treatment with TT as compared with adjuvant CPI
- Patients with distant metastases achieved favorable outcomes when switching treatments between adjuvant therapy and first-line therapy in the metastatic setting
- Response rates and survival outcomes to 1L treatments following adjuvant treatment failure were weaker compared with treatment naïve patient cohorts

Reference paper



Case study II: Real-world treatment patterns in patients with psoriasis taking systemic oral or biologic therapies

Background
- Chronic, immune-mediated, systemic inflammatory disease with prevalence of 3% in the U.S. population
- Psoriasis treatment options include topical therapies, phototherapy, and systemic oral and biologic therapies
- Moderate to severe psoriasis may require systemic therapies, whereas mild to moderate disease psoriasis can be managed with topical therapy or phototherapy

Database
- MarketScan Commercial and Medicare claims

Outcomes
- Evaluate real-world treatment patterns of switching, discontinuation, and non-switching in two cohorts of psoriasis patients initiating oral or biologic systemic therapy

Attrition

Inclusion:
- ≥1 prescription for an oral or biologic medication during index period
- ≥2 diagnosis codes(≥1 day apart) of psoriasis any time before the index date
- Continuous medical and pharmacy enrollment for ≥1 year prior to and after the index date
- Aged ≥18 years at index date

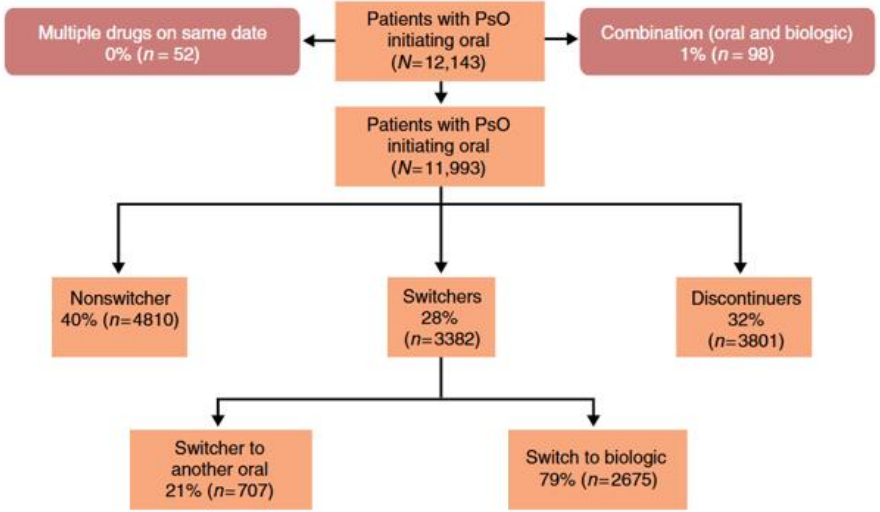
Exclusion:
- Multiple oral or biologic medication initiations on the index date or combination treatment during the index episode
- Diagnosis such as rheumatoid arthritis, psoriatic arthritis, Crohn's disease, ulcerative colitis, etc. any time before the index date

Study period: 1 January 2006 to 31 December 2019
Index period: 1 January 2013 to 31 December 2018

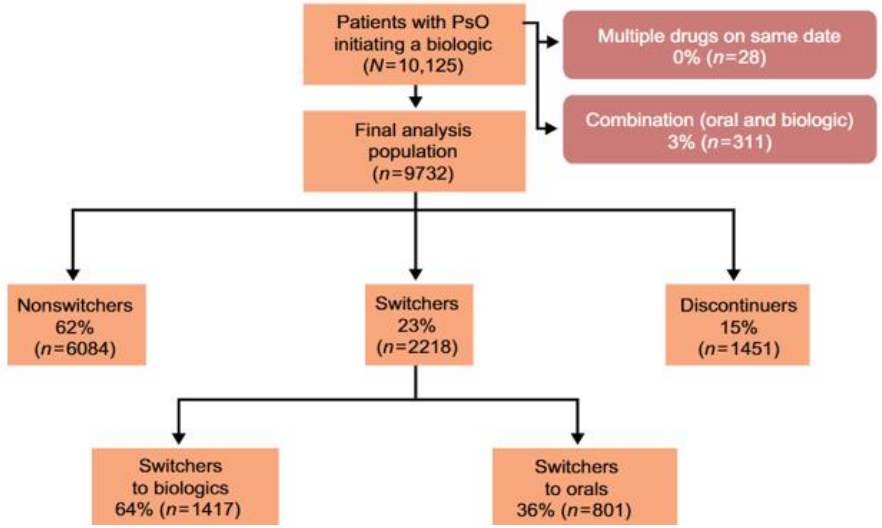
Reference paper

Case study II: Real-world treatment patterns in patients with psoriasis taking systemic oral or biologic therapies

Oral



Biologics

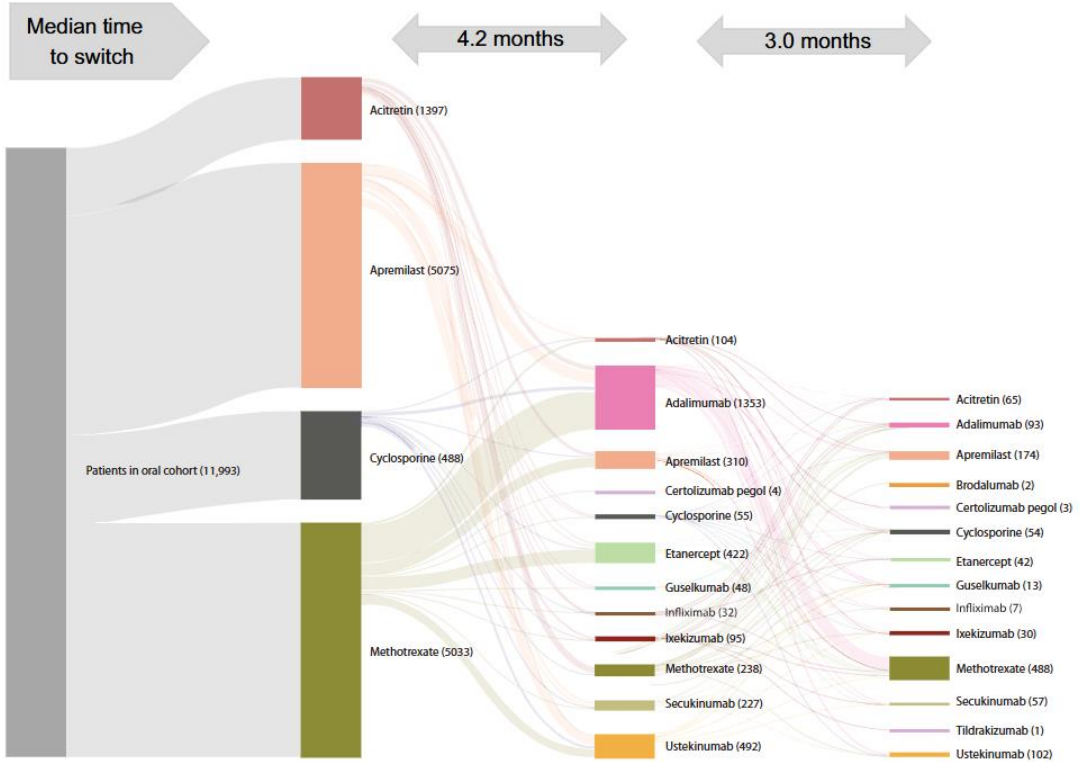


Switchers: Switched to a different drug during 1-year follow-up
Non-switchers: Remained on the index treatment during the 1-year follow-up period
Discontinuations: Prescription claim gaps of the index therapy during the 1-year follow-up period

Reference paper

Case study II: Real-world treatment patterns in patients with psoriasis taking systemic oral or biologic therapies

Sankey Diagram



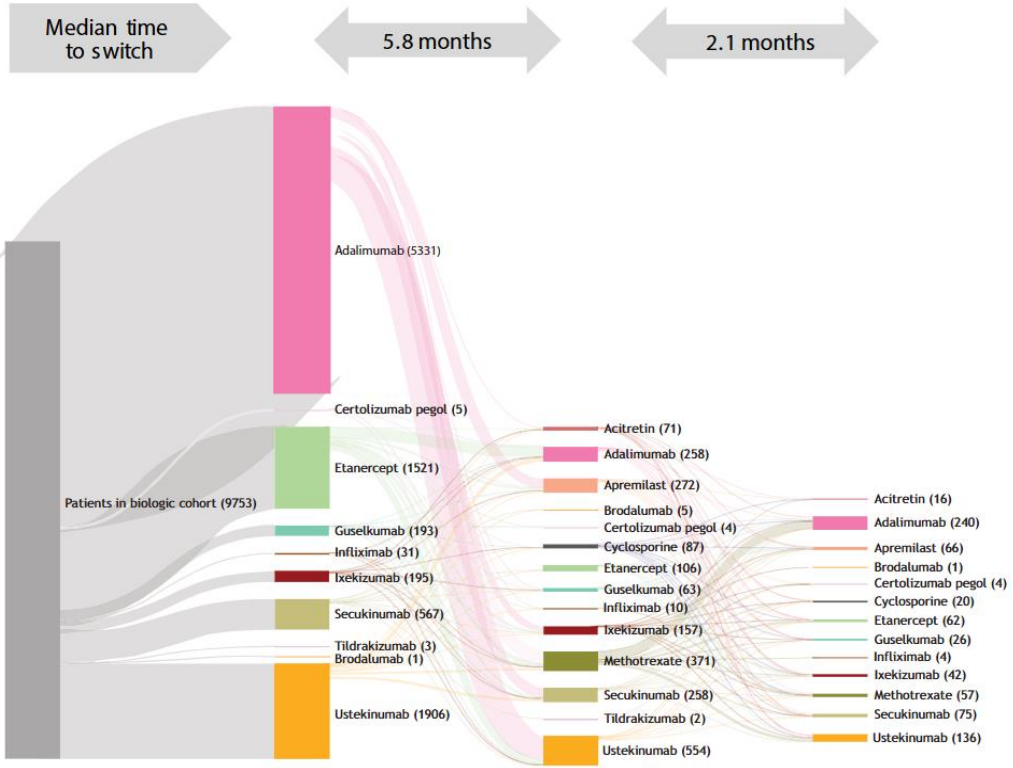
Treatment patterns of switching in the **oral** cohort (LOT 1 – 2 – 3)

Drug	LOT 1	LOT 2	LOT 3
Acitretin	1397	104	65
Adalimumab	0	1353	93
Apremilast	5075	310	174
Brodalumab	0	0	2
Certolizumab pegol	0	4	3
Cyclosporine	488	55	54
Etanercept	0	422	42
Guselkumab	0	48	13
Infliximab	0	32	7
Ixekizumab	0	95	30
Methotrexate	5033	238	488
Secukinumab	0	227	57
Tildrakizumab	0	0	1
Ustekinumab	0	492	102
Total	11,393	3380	1131

Reference paper

Case study II: Real-world treatment patterns in patients with psoriasis taking systemic oral or biologic therapies

Sankey Diagram



Treatment patterns of switching in the **biologic** cohort (LOT 1 – 2 – 3)

Drug	LOT 1	LOT 2	LOT 3
Acitretin	0	71	16
Adalimumab	5331	258	240
Apremilast	0	272	66
Brodalumab	1	5	1
Certolizumab pegol	5	4	4
Cyclosporine	0	87	20
Etanercept	1521	106	62
Guselkumab	193	63	26
Infliximab	31	10	4
Ixekizumab	195	157	42
Methotrexate	0	371	57
Secukinumab	567	258	75
Tildrakizumab	3	2	0
Ustekinumab	1906	554	136
Total	9753	2218	749

Reference paper

Case study II: Real-world treatment patterns in patients with psoriasis taking systemic oral or biologic therapies

Observations:
Oral cohort:
- 40% patients remained on index therapy, 28% switched, whereas 32% of patients discontinued. Majority switches (79%) were to biologics
- Most common index medication - Apremilast (42%); least common - Cyclosporine (4%)
- Most common second-line therapies was biologics Adalimumab, followed by Ustekinumab and Etanercept

Biologic cohort:
- 62% patients remained on index therapy, 23% switched, whereas 15% of patients discontinued. Majority switches were to another biologics
- Most common index biologics was Adalimumab(55%), followed by Ustekinumab and Etanercept
- Most common second-line therapies was biologics Ustekinumab, followed by oral therapies Methotrexate and Apremilast

Conclusions:
- Treatment persistence was low within the first year of starting a systemic therapy
- Almost one fourth of the oral (28%)and biologic (23%) treatment cohorts switched from their index therapy
- Among patients who did not discontinue, 41% of oral initiators and 27% of biologic initiators switched treatment
- Despite multiple treatments, there exists an unmet need for effective first-line treatments, particularly oral therapies

Reference paper

Conclusion

- RWE is revolutionizing clinical research by offering real world insights into treatment efficacy, safety, and patient outcomes
- Kaplan Meier curves and Sankey diagrams helps visualize complex RWD and generate actionable insights supporting regulatory decisions and improving patient care

Challenges:

- Real-world datasets often include missing data, inconsistent coding, or incorrect diagnoses
- KM curves are limited to determine effect of multiple covariates at a time
- Sankey diagrams become overcrowded and hard to interpret when dealing with large datasets

Future directions:

- ML and AI driven analysis to generate more accurate survival predictions
- Interactive Sankey Diagrams

Reference paper

References

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