Review Article

Biologics and Immunomodulators in Current Use for Major Clinical Diseases and Malignancies

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Abstract

With the dramatic increase in biologics and immunomodulators currently being used to treat multiple diseases and malignancies in areas such as rheumatology, dermatology, gastroenterology, ophthalmology and hematology to name a few, these authors have sought out to analyze and summarize the incredible amount of available FDA approved biologics and immunomodulators in order to improve awareness of their mechanisms and indications in hopes of improving medical decision making. The increased complexity of patients with multiple comorbidities requires physicians and other healthcare providers to be aware of multiple treatment options to tailor treatment accordingly. We have delineated receptor targets and have pointed out the overlap of biologics and immunomodulators in the treatment of multiple clinically important diseases and malignancies.

Keywords: Immunomodulators; Patients; Rheumatology; Dermatology; Gastroenterology; Ophthalmology

Introduction

The clinician today can be overwhelmed with the multitude of biologics and immunomodulators that are available to treat clinically important diseases and malignancies. An immunomodulator is a molecular compound that in general can upregulate or downregulate an immune response. It is used to treat multiple conditions including infectious diseases, autoimmune disorders, malignancies and hypersensitivity reactions [1]. A biologic is a type of biologically derived compound composed of molecules from bacteria, humans and other animals used to target bioactive receptors to either upregulate or downregulate their actions. A biologic can be a type of specified immunomodulator [2].

The genesis of this research paper was sparked by the need for understanding the overlapping uses of current biologics and immunomodulators. There are many circumstances where overlapping clinical diseases can be treated by the same biologic and/or immunomodulator. For instance, psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn's Disease and ulcerative colitis can all be treated with the same biologic class-tumor necrosis blocking agents such as adalimumab [3]. As well, there are many circumstances where biologics and immunomodulators can treat both malignancies and clinical diseases. For instance, rituximab can treat B-cell non-hodgkin's lymphoma a malignant condition and granulomatosis with polyangiitis, pemphigus vulgaris, Rheumatoid Arthritis (RA) and systemic lupus erythematosus all non-malignant diseases [4]. Imiquimod cream is yet another example of this crossover which is used to treat superficial basal cell carcinoma, Actinic Keratoses (AKs), condyloma acuminata and has also been used as adjuvant therapy in Melanoma *in-situ* when margins are hard to obtain from a surgical excision [5,6].

Another prime example is the use of an IL4 and IL13 blocking agent dupilumab, that can be used to treat atopic dermatitis, prurigo nodularis, nasal polyposis, eosinophilic esophagitis, eosinophilic gastroenteritis and bullous pemphigoid to name a few [7].

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Methods

Biologics and immunomodulators were reviewed on the FDA biological approval lists and the National Library of Medicine DrugBank. Once the biologics and immunomodulators were identified, FDA-approved prescribing information was reviewed to determine their mechanisms and indications. The review was conducted from 18 December 2024 through 3 March 2025. Seventeen researchers participated in the search process.

Results

Clinical Diseases

There are 133 biologics and immunomodulators that target 70 receptors and that treat 115 clinical diseases (Fig. 1-14).

Malignant Diseases

There are 193 biologics and immunomodulators that target 61 receptors and that treat 475 malignant diseases.

At the time of writing this research paper including the important clinical diseases and malignancies, there were 557 clinically important diseases that were treated with approximately 327 biologics with approximately 108 targeted receptors.
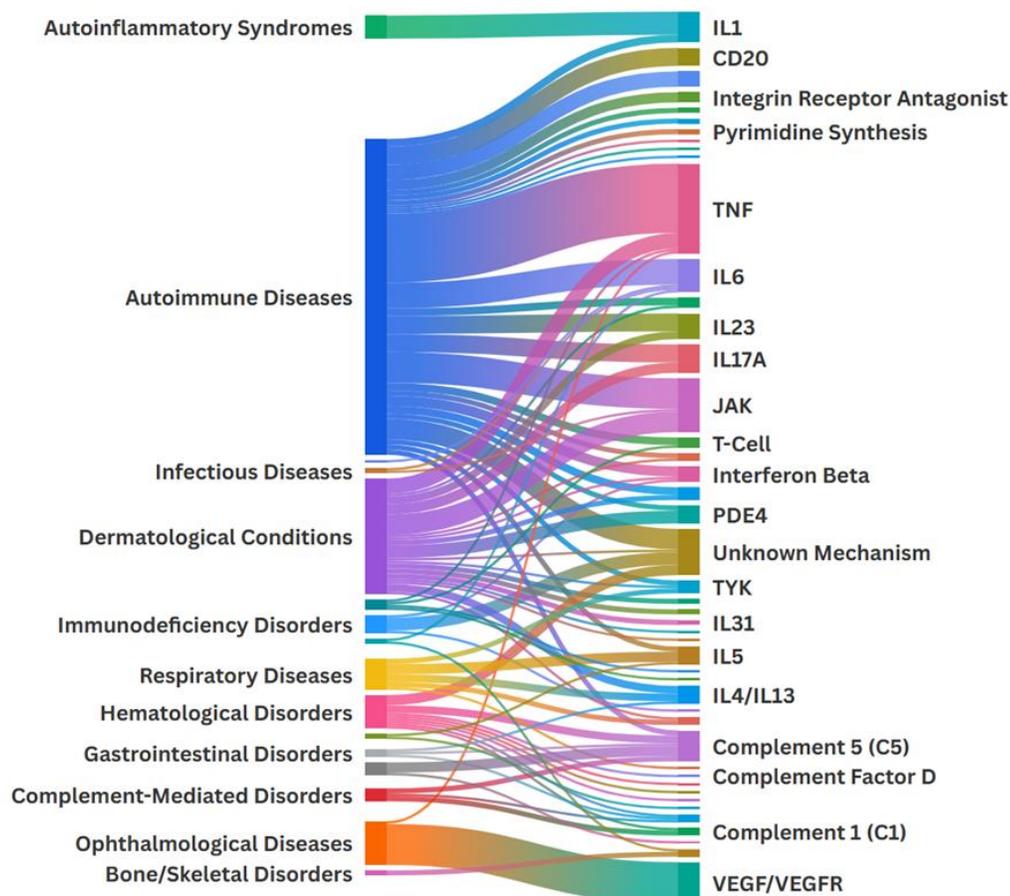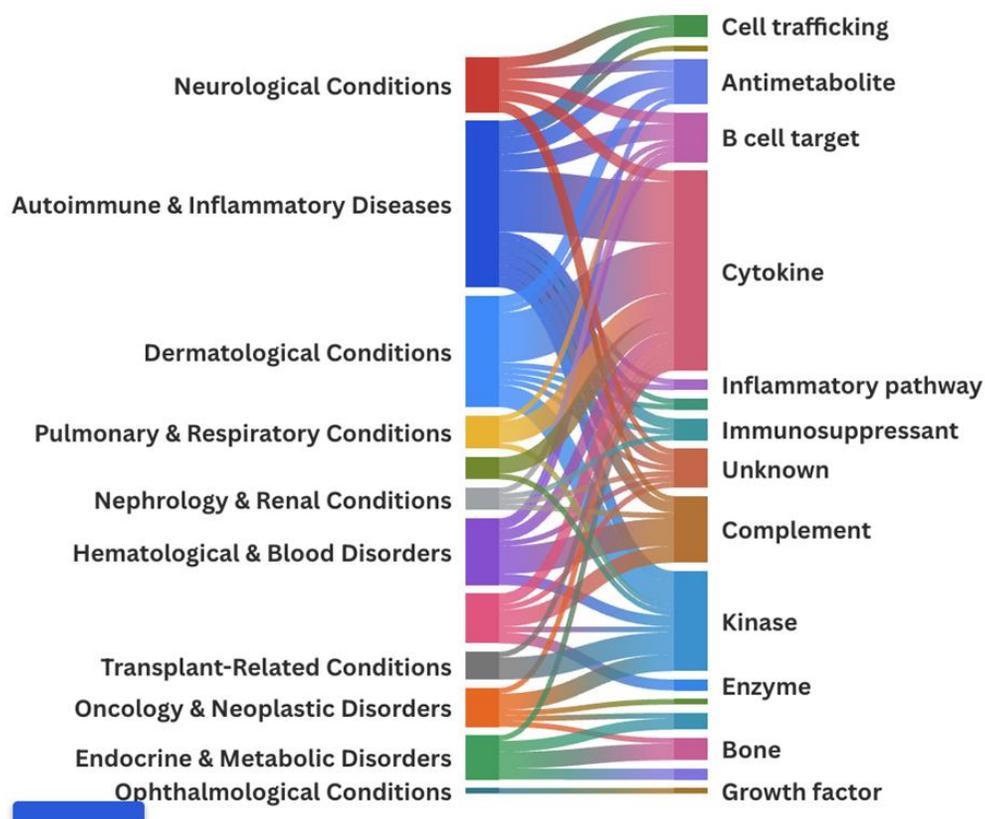
Figure 1: Nonmalignant.

The chart below is a Sankey graph that shows the clustering of groups of non malignant diseases and their respective receptor targets. It is interesting to note that the majority of targeted diseases were in the category of autoimmune, followed by dermatological diseases, followed by ophthalmological diseases.
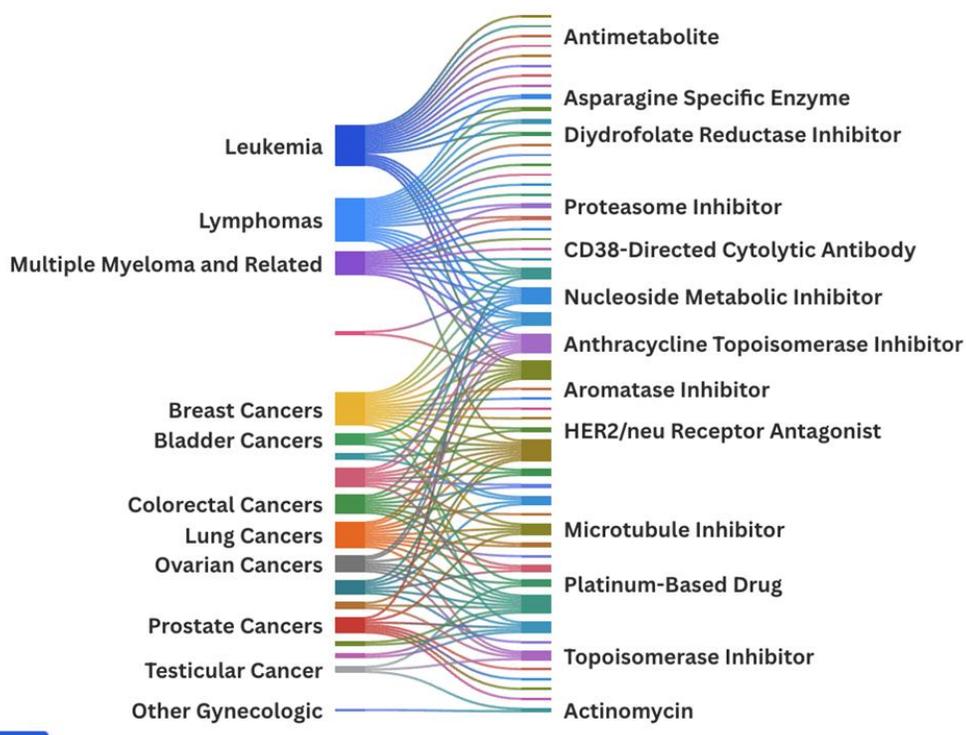

Figure 2: Malignant.

The chart below is a Sankey graph that shows the clustering of groups of malignant diseases and their respective receptor targets. The majority of targeted diseases were in the category of lymphoproliferative disorders.

Non-Malignant Data

Figure 3: Top 20 Non Malignant Diseases Treated by FDA Approved Biologics/Immunomodulators.

Indicates the number of FDA-approved biologic and immunomodulator treatment options available for the top 20 non-malignant diseases.

Figure 4: Top 35 most indicated biologics and immunomodulators for non-malignancies.

Indicates the most indicated biologics and immunomodulators based on the number of different diseases or conditions they can treat. Particularly, Adalimumab, offers significant advantages in terms of treatment flexibility and potential for addressing multiple comorbid conditions in patients with complex autoimmune disease profiles. In the category of most indicated biologics and immunomodulators for non-malignancies, the top 8 with the most indications were Adalimumab (11), Upadacitinib (9), Canakinumab (8), Dupilumab (8), Etanercept (8), Infiximab (8), Certolizumab pegol (7) and Tocilizumab (7), respectively.
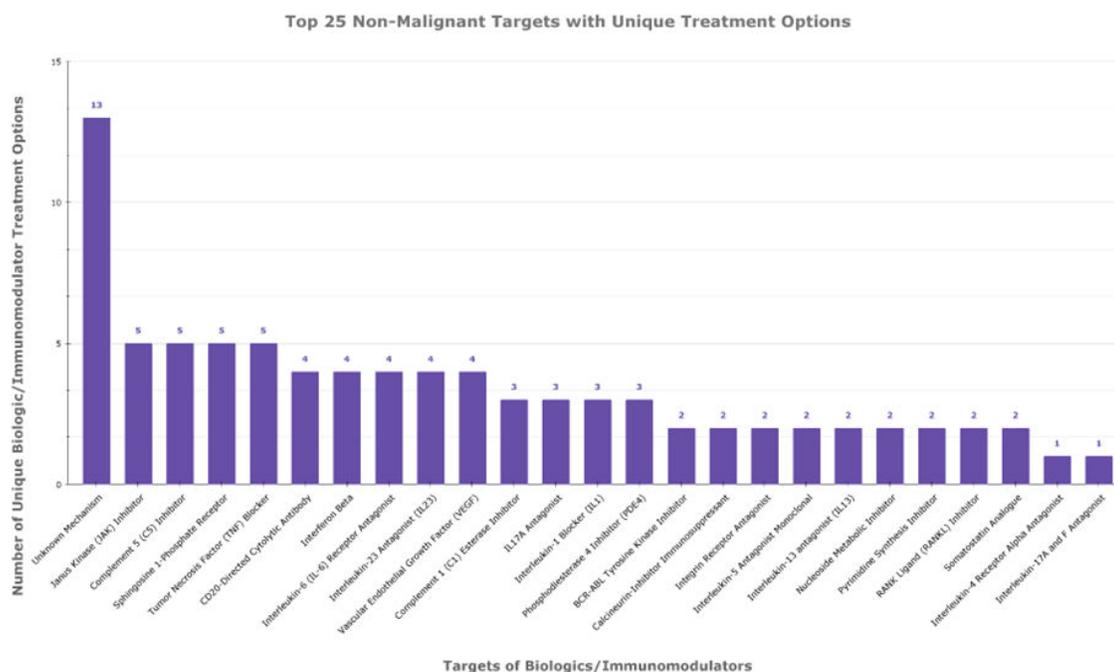

Figure 5: Top 25 non-malignant targets with unique treatment options.

Indicates the therapeutic targets for non-malignant diseases most commonly addressed by FDA-approved biologics and immunomodulators.
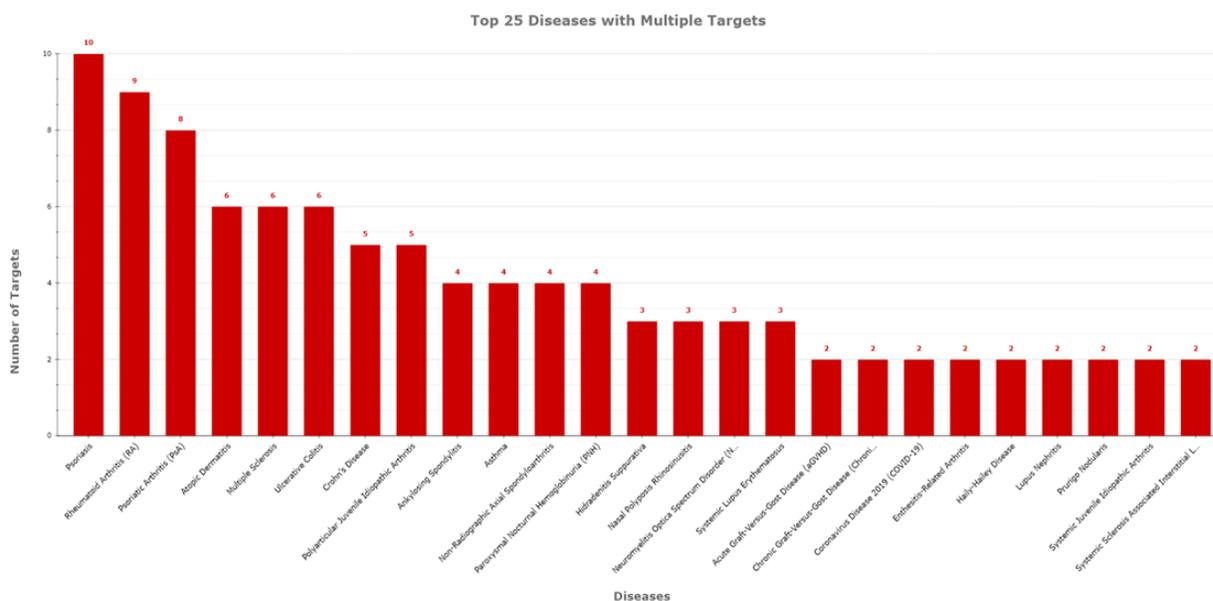

Figure 6: Top 25 non-malignant diseases with multiple targets.

Non malignant diseases that are treated with multiple targets.

Figure 7: Top 30 targets treating multiple non-malignant diseases.

Diseases that can be treated through multiple therapeutic targets, illustrating the complexity and diversity of treatment options that are available for each condition. Fig. 8 indicates the FDA approval trends for biologics and immunomodulators used to treat non-malignant conditions from 1950 to 2025. The data shows an acceleration in approvals over time. The light blue trend line shows a clear upward trajectory with the equation $y = 0.13x + 0.666$, indicating steady growth over the decades. The R^2 value of 0.458 suggests a moderate correlation. The biologics and immunomodulator field has evolved from a niche area with sporadic approvals to a major therapeutic option for prescribing clinicians and patients. This trend represents a shift towards targeted therapies in response to complex immune conditions.

Figure 8: Approval dates of biologics and immunomodulators treating non-malignant diseases from 1950-now.
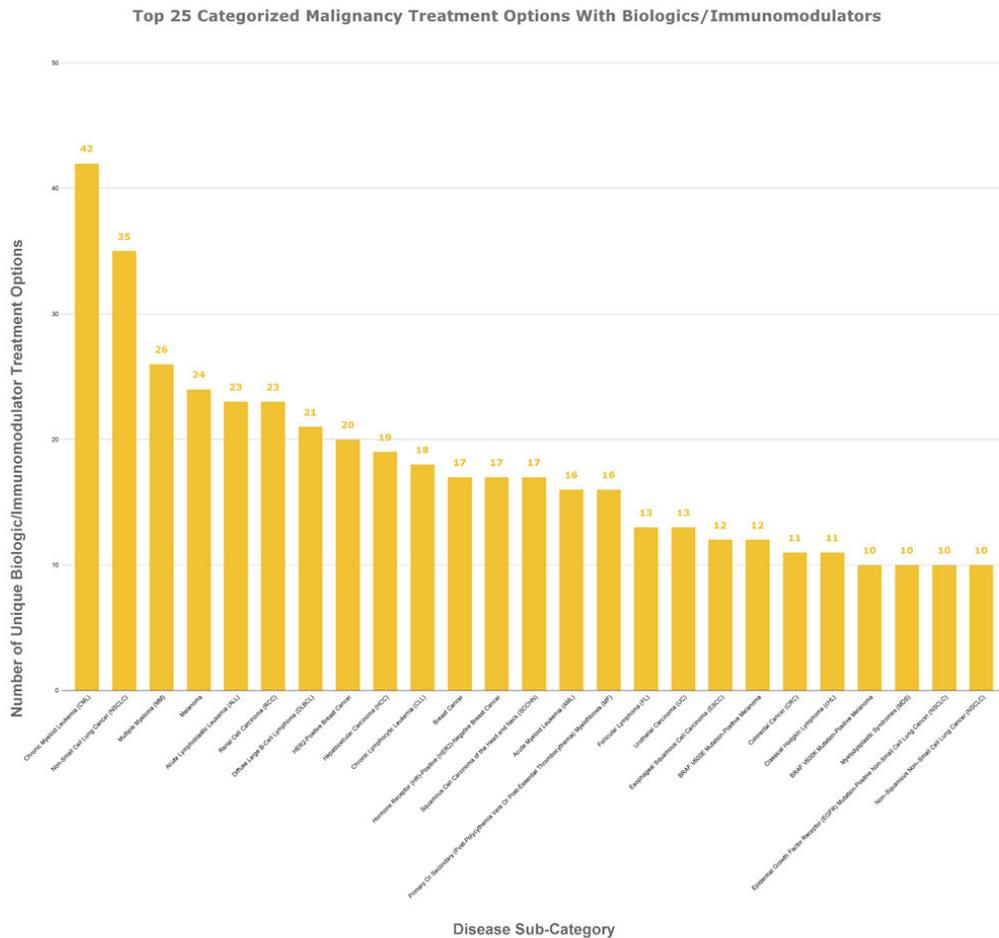
Malignant Data

Figure 9: Top 25 categorized malignancy treatment options with biologics and immunomodulators.

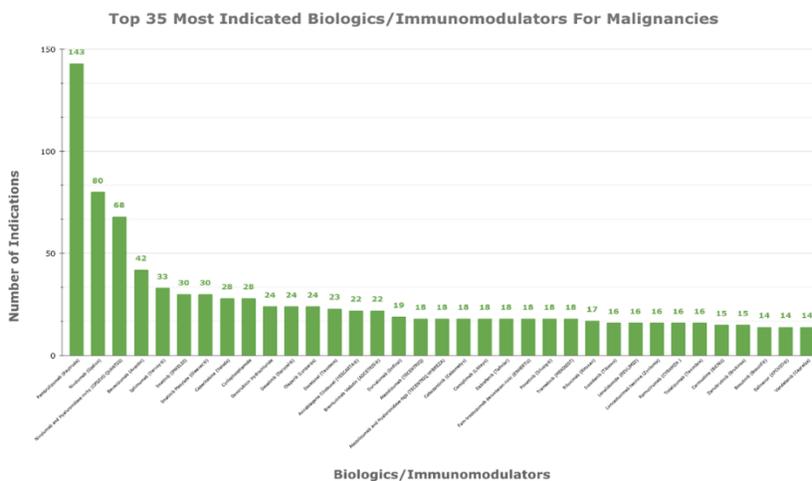The number of FDA-approved biologic and immunomodulator treatment options available for the top 25 malignant diseases.

Figure 10: Top 35 most indicated biologics and immunomodulators for malignancies.

The most indicated biologics and immunomodulators based on the number of different diseases or conditions they can treat.
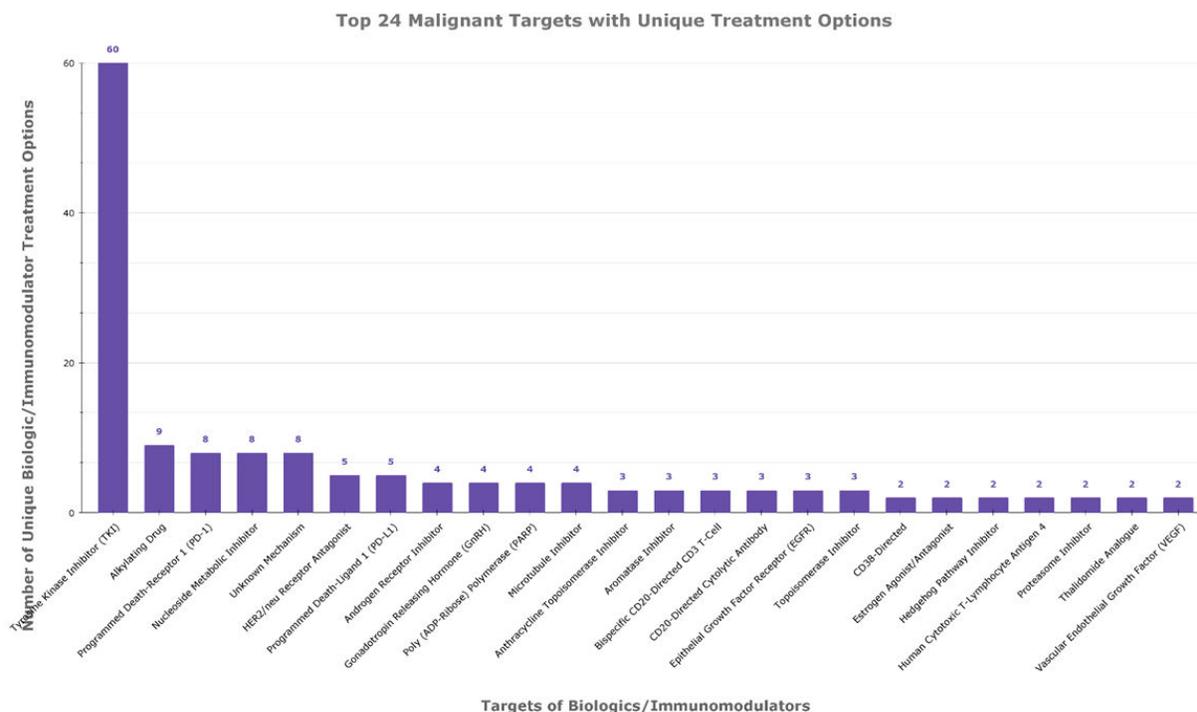
Top 24 Malignant Targets with Unique Treatment Options

Figure 11: Top 24 targets treated by fda approved biologics and immunomodulators.

Therapeutic targets for malignant diseases most commonly addressed by FDA-approved biologics and immunomodulators.
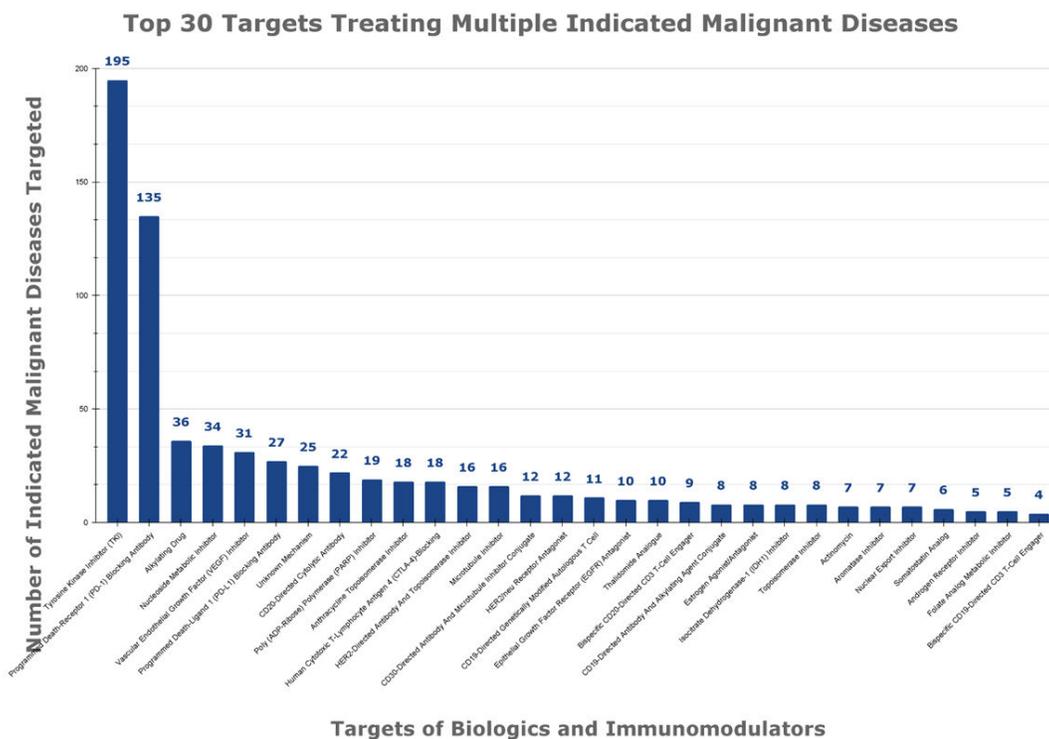
Top 30 Targets Treating Multiple Indicated Malignant Diseases

Figure 12: Top 30 malignant diseases with multiple targets.

The biologic and immunomodulator targets that demonstrate the highest indications in treating multiple malignant diseases.
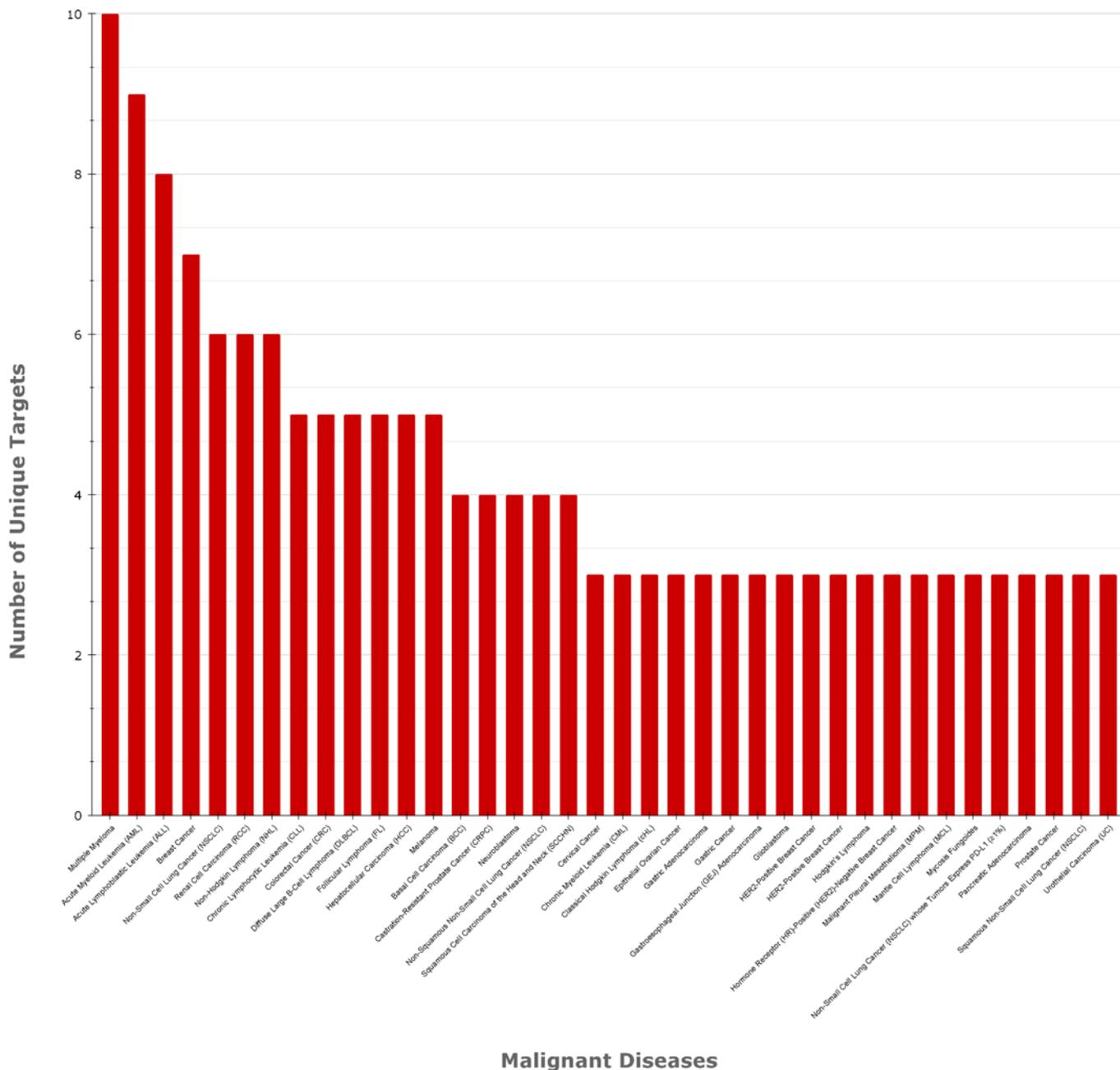

Figure 13: Top 38 malignant diseases with unique drug targets.

Indicates the malignant diseases that can be treated through multiple therapeutic targets.
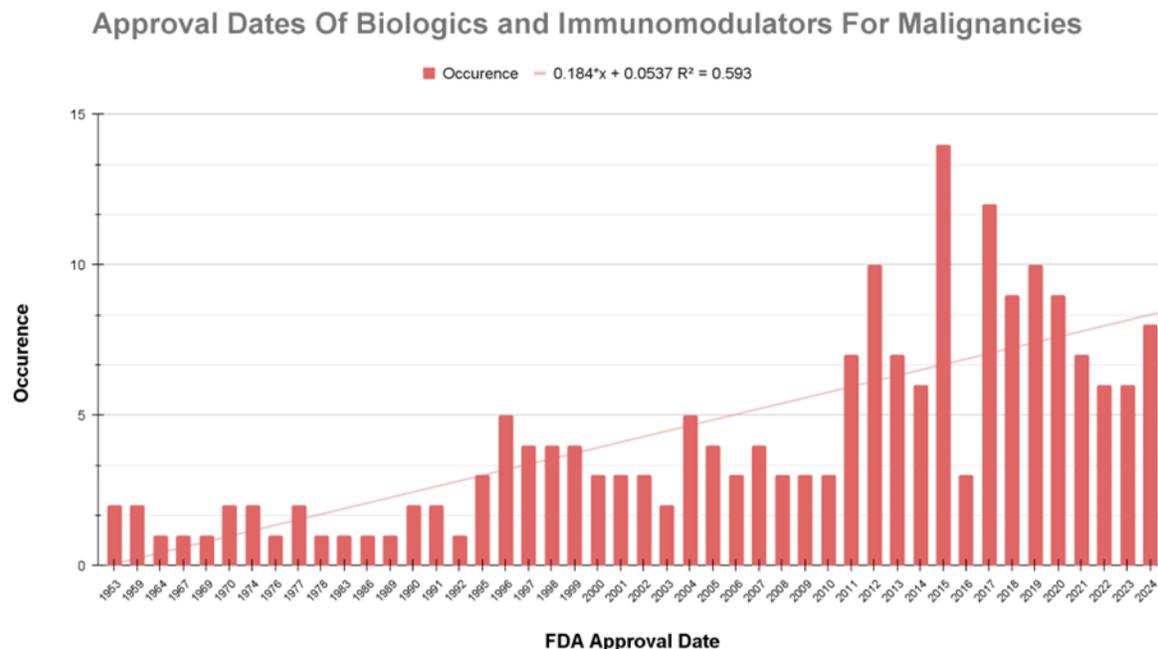
Figure 14: Approval dates of biologics and immunomodulators treating malignant diseases from 1953-now.

FDA approval trends for biologics and immunomodulators used to treat malignant conditions from 1953 to 2024. Compared to non-malignant diseases, there is more significant growth and greater approval volumes. The light red trend line (y = 0.184x + 0.0537) shows a steeper slope than the non-malignant chart, with a higher R^2 value of 0.593, indicating a stronger correlation.

Discussion

At this time, there are numerous biologics and immunomodulating drugs on the market that address multiple non-malignant and malignant conditions. These drugs have the ability to target multiple conditions simultaneously- even malignant and non malignant conditions. Increased research on these medications is expanding the FDA approved indications making them more versatile. As medications and patients' conditions become more complex, clinicians will have to remain up to date with the advancements in FDA approved indications in order to match the right drug to the patient's multiple comorbidities.

Upon completing the research and placing it in charts/tables/graph-format the data revealed many important patterns. What is most striking about the data is an overwhelming abundance of autoimmune diseases that are treated, followed by dermatologic conditions followed by ophthalmologic diseases, then hematologic disorders (Fig. 1). Fig. 2 shows clustering of groups of malignant diseases and their respective receptor targets. It is interesting to note that the majority of targeted diseases were lymphoproliferative malignancies, mainly lymphomas and leukemias, followed by breast cancer, lung cancer and multiple myelomas.

What is also extremely important is the interconnection of diseases and the overlap of treatment options with these diseases. The following biologics are examples of one biologic able to treat multiple diseases across different specialties [9]. They are not the exception but examples, as there are many more biologics/immunomodulators that treat more than one disease. Adalimumab (Humira) a TNF blocker treats rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, hidradenitis suppurativa, Crohn's disease, ulcerative colitis,chronic plaque psoriasis and non-infectious intermediate, posterior panuveitis [3].

Baricitinib (Olumiant) which is a JAK inhibitor treats alopecia areata, rheumatoid arthritis and COVID-19 [8]. Imatinib (Gleevec, Imkeldi)) which is a tyrosine kinase inhibitor treats chronic myelogenous leukemia, acute lymphoblastic leukemia,gastrointestinal stromal tumors, myelodysplastic/myeloproliferative diseases, aggressive systemic mastocytosis, hypereosinophilic syndrome, chronic eosinophilic leukemia and dermatofibrosarcoma protuberans [9].

Ravulizumab-cwyz (Ultomiris) which is a complement inhibitor that treats paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, myasthenia gravis and neuromyelitis optica spectrum disorder [10]. Rituximab (Rituxan) which is a CD20 directed cytolytic antibody treats rheumatoid arthritis, granulomatosis with polyangiitis, microscopic polyangiitis, pemphigus vulgaris, non hodgkin's lymphoma and chronic lymphocytic leukemia [4].

Secukinumab (Cosentyx) which is a human interleukin 17a antagonist that treats plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, enthesitis-related arthritis and hidradenitis suppurativa [11]. Tocilizumab (Actemra) which is an interleukin 6 receptor antagonist treats giant cell arteritis, systemic sclerosis associated interstitial lung disease, polyarticular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, cytokine release syndrome and coronavirus disease 2019 [12]. Tofacitinib (Xeljanz) which is a Janus kinase inhibitor treats rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, ulcerative colitis, juvenile idiopathic arthritis [13]. There were 18 biologic/immunomodulator overlaps of shared receptors for malignant and non malignant conditions (Table 1).

Azacitidine (Vidaza)
Carmustine (BiCNU)
Daratumumab and Hyaluronidase-fihj (DARZALEX FASPRO®)
Everolimus (AFINITOR®)
Fluorouracil (5FU)
Ibrutinib (Imbruvica)
Imatinib (IMKELDI)
Imatinib Mesylate (Gleevec®)
Imiquimod (Imiquimod)
Interferon Gamma-1b (ACTIMMUNE)
Lanreotide (Somatuline)
Methotrexate
Ofatumumab (ARZERRA®)
Pamidronate Disodium (Aredia®)
Rituximab (Rituxan)
Ruxolitinib (Jakafi)
Thalidomide (THALOMID)
Zoledronic Acid (Zometa)

Table 1: 18 biologic/immunomodulator overlaps.

There were 61 unique targets used to treat malignant diseases and 70 unique targets to treat non-malignant diseases. In total there were 131 targets. In the category of non-malignant disease treatment options, the top 7 non-malignant diseases with the most unique biologic/immunomodulator treatments are Psoriasis (19), Multiple Sclerosis (18), Rheumatoid Arthritis (18), Psoriatic Arthritis (15), Ulcerative Colitis (13), Ankylosing Spondylitis (10) and Atopic Dermatitis (10), respectively (Fig. 1).

In the category of most indicated biologics and immunomodulators for non-malignancies, the top 8 with the most indications were Adalimumab (11), Upadacitinib (9), Canakinumab (8), Dupilumab (8), Etanercept (8), Infiximab (8), Certolizumab pegol (7) and Tocilizumab (7), respectively (Fig. 2).

In the category of unique treatment options for non-malignant targets, the top 5 with the most number of unique biologics/immunomodulators were Unknown mechanism (13), Janus Kinase JAK inhibitor (5), Complement 5 (C5) Inhibitor (5), Sphingosine 1-Phosphate Receptor (5) and Tumor Necrosis Factor (TNF) Blocker (5), respectively (Fig. 3).

In the category of non malignant diseases that were treated with multiple targets, the top 6 diseases were Psoriasis (10), Rheumatoid Arthritis (9), Psoriatic Arthritis (8), Atopic Dermatitis (6), Multiple Sclerosis (6) and Ulcerative Colitis (6), respectively (Fig. 4).

In the category of top 30 targets treating multiple non-malignant disease, the top 5 with the most number of non-malignant diseases targeted were Tumor Necrosis Factor (TNF) (14), Interleukin-1 Blocker (IL1) (13), Janus Kinase (JAK) Inhibitor (13), Interleukin-6 (IL-6) Receptor Antagonist (10) and Unknown Mechanism (10), respectively (Fig. 5).

The approval dates of biologics and immunomodulators treating non-malignant diseases from 1950-now displays that there is a significant increase in FDA approvals starting in 2009 all the way through 2024, with an approximate average of 5.73 approvals per year in that time period (Fig. 6).

In the category of malignancy treatment Options With Biologics and Immunomodulators, the top 6 with the most number of unique biologics/immunomodulator treatment options were Chronic Myeloid Leukemia (CML) (42), Non-Small Cell Lung Cancer (NSCLC) (35), Multiple Myeloma (26), Melanoma (24), Acute lymphoblastic leukemia (ALL) (23) and Renal Cell Carcinoma (RCC) (23), respectively (Fig. 7).

In the category of most indicated biologics and immunomodulators for malignancies, the top 5 with the most number of indications were Pembrolizumab (Keytruda) (143), Nivolumab (Opdivo) (80), Nivolumab and Hyaluronidase-nvhy (OPDIVO Qvantig) (68), Bevacizumab (Avastin) (42) and Ipilimumab (Yervoy) (33), respectively (Fig. 8).

In the category of therapeutic targets for malignant diseases, the top 5 most commonly addressed by FDA-approved biologics and immunomodulators were Tyrosine Kinase Inhibitor (TKI) (60), Alkylating Drug (9), Programmed Death-Receptor 1 (PD-1) (8), Nucleoside Metabolic Indicator (8) and Unknown Mechanism (8), respectively (Fig. 9).

In the category of biologic and immunomodulator targets, the top 5 treatments that demonstrate the highest indications in treating multiple malignant diseases were Tyrosine Kinase Inhibitor (TKI) (195), Programmed Death-Receptor 1 (PD-1) Blocking Antibody (135), Alkylating Drug (36), Nucleoside Metabolic Indicator (34) and Vascular Endothelial Growth Factor (VEGF) Inhibitor (31), respectively (Fig. 10).

In the category of malignant diseases that can be treated through multiple therapeutic targets, the top 5 unique treatments Multiple Myeloma (10), Acute Myeloid Leukemia (AML) (9), Acute Lymphoblastic Leukemia (8), Breast Cancer (7), Non-Small Cell Lung Cancer (NSCLC) (6), Renal Cell Carcinoma (RCC) (6), Non-Hodgkins Lymphoma (NHL) (6), respectively (Fig. 11).

The approval dates of biologics and immunomodulators treating malignant diseases from 1953 through 2024 displays that there is an increase in FDA approvals starting in 2011 all the way through 2024, with an approximate average of 8.76 approvals per year in that time period (Fig. 12) [14].

Conclusion

This paper is by all means not a comprehensive list, we encourage the reader to get more specific prescribing information when they are contemplating the use of these biologics and immunomodulators. We attempted to succinctly show their usage and receptors and cross use in a palatable format. This research has shown the explosion of biologics within the last five years. This will necessitate frequent updating of this research. Currently, the logarithmic growth of medical knowledge has allowed further and deeper understanding of the pathophysiology at the molecular level to treat many of these diseases. Hence the biologics we predict in the future will be even more abundant as more knowledge becomes apparent, whether by thinking scientists or a combination of bench scientific research and artificial intelligence modeling. Currently there are multiple companies that are engaged in artificial intelligence modeling to develop new drugs. With further research and the delineation of more specific targets, there will be a better understanding of the treatment capabilities which will lead to multiple diseases being treated by the same biologics and immunomodulators. This will then lead to more efficient treatment and lower cost. Our research has shown the proliferation of biologics/immunomodulators within the last five years with 68 biologics/immunomodulators having been FDA approved. The trend has been explosive and we anticipate more approvals for malignant and nonmalignant conditions.The authors anticipate an overlap of efficacy amongst many classes of diseases. Hence a clinician/researcher should vigorously search whether or not the disease they are treating could also treat other conditions the patient is diagnosed with. This should simplify therapeutics, reduce waste, additional cost and time in treating these diseases.

The growth of medical knowledge has allowed further and deeper understanding of the pathophysiology at the molecular level to treat many of these diseases. With further research and the delineation of more specific targets, there will be a better understanding of the treatment capabilities which will lead to even more overlap between disease therapeutics.

Conflict of Interest

The author declares no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Author's Contribution

Author read and approved the final manuscript.

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