Anti-amyloid therapies and the transformation of Alzheimer's care pathways: early lessons from the frontline

Massimo Filippi,[a,b,c,d,e,*] Giordano Cecchetti,[a,b] Edoardo G. Spinelli,[a,b,c] Alma Ghirelli,[a,b,c] Giulia Rugarli,[a,b,c] Stefano Pisano,[a,b] Elisa Canu,[a,b] and Federica Agosta[a,b,c,e]

[a]Center for Alzheimer's and Related Diseases (CARD), Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[b]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
[c]Vita-Salute San Raffaele University, Milan, Italy
[d]Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
[e]Neurotech Hub, Vita-Salute San Raffaele University, Milan, Italy

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Summary

The introduction of anti-amyloid monoclonal antibodies marks a major shift in Alzheimer's disease (AD) care, moving treatment toward biological modification and reshaping diagnostic and organizational models. At the Center for Alzheimer's and Related Diseases (CARD), IRCCS San Raffaele Hospital (Milan, Italy), among the first European tertiary centers to initiate both lecanemab and donanemab, we developed a structured fast-track pathway to support timely and safe access to therapy. Our early real-world experience highlights three critical domains. First, patient selection requires integration of cognitive, functional, and biological data, moving beyond rigid global score thresholds. Second, safety monitoring must balance ARIA risk with real-world feasibility through risk-adapted MRI surveillance. Third, effective implementation depends on transparent communication and continuous shared decision-making, particularly when benefit is uncertain or safety events occur. These elements underscore that the impact of disease-modifying therapies will depend not only on pharmacology, but on coordinated care models supported by real-world registries.

Keywords: Alzheimer's disease; Anti-amyloid therapy; Donanemab; Lecanemab; Real-world implementation

Introduction

For decades, the treatment of Alzheimer's disease (AD) was limited to symptomatic strategies, with limited impact on disease progression. The recent approval of anti-amyloid monoclonal antibodies for early symptomatic AD marks a historic shift toward biological disease modification. Pivotal trials of lecanemab and donanemab demonstrated that amyloid removal can slow cognitive and functional decline, redefining therapeutic expectations.[1,2]

In Europe, the transition from research to clinical practice is now underway, following European Medicine Agency (EMA) approval of both agents in 2025.[3,4] However, real-world evidence on feasibility, safety, and early biological effects remains limited.[5–7] Integrating these therapies into healthcare systems requires substantial reorganization of diagnostic pathways, monitoring structures, and resource allocation, changes extending well beyond pharmacology.

*Corresponding author. Neurology Unit, IRCCS San Raffaele Scientific Institute, Via Olgettina, 60, 20132, Milan, Italy.

E-mail addresses: filippi.massimo@hsr.it (M. Filippi), cecchetti.giordano@hsr.it (G. Cecchetti), spinelli.edoardogioele@hsr.it (E.G. Spinelli), ghirelli.alma@hsr.it (A. Ghirelli), rugarli.giulia@hsr.it (G. Rugarli), pisano.stefano@hsr.it (S. Pisano), canu.elisa@hsr.it (E. Canu), agosta.federica@hsr.it (F. Agosta).

At the IRCCS San Raffaele Center for Alzheimer's and Related Diseases (CARD, Milan, Italy), a high-volume referral center, we were among the first European institutions to introduce both antibodies into routine care under EMA-aligned safety protocols and multidisciplinary oversight. We established a dedicated programme based on Appropriate Use Recommendations (AURs) and Committee for Medicinal Products for Human Use (CHMP) indications.[3,4,8,9]

Both therapies are currently administered through a named-patient importation program, in accordance with the Italian Ministerial Decree of February 11, 1997, allowing access prior to full national reimbursement pathways. Under this framework, costs cannot be charged to the National Health Service and are therefore borne directly by patients.

As of 12 November 2025, 32 patients have initiated treatment at CARD, for a total of 33 prescriptions: 8 with lecanemab, 23 with donanemab, and 1 individual switched from lecanemab to donanemab.

Drawing on this frontline experience, this personal view summarizes early lessons from the first year of implementation, outlining the evolving patient journey, key organizational requirements, and emerging clinical questions that define this new therapeutic era. Our aim

is to offer a framework for safe, equitable, and patient-centered integration of disease-modifying therapies into AD care.

Fast-track implementation pathway for anti-amyloid therapy

The introduction of disease-modifying therapies has reshaped diagnostic pathways for AD, shifting them from a traditionally sequential model to a biologically anchored and time-sensitive workflow.

The patient journey at our center begins with Assessment 1, either through standard referral or via a dedicated telemedicine-based pre-screening pathway (Fig. 1). The latter was implemented to accelerate access for individuals potentially eligible for anti-amyloid therapy. Remote triage consists of a structured clinical interview with the patient and an informant, review of available clinical documentation (including prior cognitive testing, MRI, and plasma/cerebrospinal fluid [CSF] biomarkers when present), and systematic screening for major contraindications such as anticoagulant use, significant psychiatric or neurological comorbidities, immunosuppressive therapies, or MRI infeasibility. This upstream filter helps determine whether the clinical presentation is compatible with early symptomatic AD and identifies candidates who should proceed to in-person evaluation. Since its activation in December 2024, the telemedicine triage system has handled approximately 80 referral requests, with about 18–20% proceeding to in-person evaluation.

Assessment 2 involves an in-person cognitive and neurological examination, providing the clinical context required to interpret biomarker findings. Cognitive status is assessed using the Clinical Dementia Rating (CDR and CDR-SB),[10] the Mini-Mental State Examination (MMSE),[11] the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog),[12] and the Alzheimer's Disease Cooperative Study–Mild Cognitive Impairment–Activities of Daily Living (ADCS MCI–ADL) scale,[13] complemented by domain-specific neuropsychological tests evaluating attention/executive function, memory, language, visuospatial abilities, praxis, and functional performance.

Assessment 3 combines structural MRI with plasma biomarkers. MRI assesses key exclusion criteria, including microbleeds, cortical superficial siderosis, and other competing pathologies, while plasma pTau-217 (alone or expressed as a pTau-217/Aβ42 ratio), together with the Aβ42/40 ratio, provides an early biological anchor supporting diagnostic coherence with AD pathology and guiding prioritization of confirmatory testing.

Although plasma biomarkers substantially streamline the diagnostic workflow, their interpretation requires awareness of several constraints. Pre-analytical factors (sample handling, delays in processing, matrix effects) and assay-related variability across platforms can influence absolute concentrations, and cross-laboratory harmonization is still evolving.[14] Moreover, regulatory validation remains incomplete in Europe, and contextual interpretation is essential in older adults or individuals with comorbidities (particularly renal dysfunction) where specificity may be reduced.[14]

When the overall picture remains consistent with AD, Assessment 4 is performed during the same visit to avoid delays. Apolipoprotein E (ApoE) genotyping is obtained systematically for risk stratification, and CSF analysis is performed when not contraindicated and when not previously available.

This sequencing reflects both biological and practical considerations: CSF represents the most informative confirmatory test in our setting, as it enables simultaneous assessment of Aβ42/40, phosphorylated tau, and total tau, thereby supporting biological staging within the AT(N) framework.[15] CSF is also substantially more accessible than amyloid PET in Italy, with shorter waiting times and lower logistical burden. MRI is obtained beforehand for procedural safety and to ensure diagnostic coherence before moving to invasive testing. For these reasons, CSF constitutes the preferred confirmatory tool when feasible, whereas amyloid PET is reserved for the final pre-treatment phase to quantify baseline amyloid burden rather than to establish diagnosis.

Assessment 5 consists of two sequential steps. First, a shared decision-making session addresses expected benefits, amyloid-related imaging abnormalities (ARIA) risks, treatment logistics, and the anticipated trajectory of care. Baseline amyloid PET imaging is then performed only after informed consent in all patients willing to proceed to treatment, providing a quantitative reference of amyloid burden before therapy initiation.

Importantly, this accelerated pathway applies only to individuals potentially eligible for anti-amyloid treatment. Patients who do not meet preliminary treatment criteria continue along the standard comprehensive diagnostic pathway used in our center, which includes full clinical, neuropsychological, and biomarker assessment according to current guidelines. The fast-track model therefore complements (rather than replaces) the routine diagnostic workflow, ensuring biological confirmation for all patients while prioritizing timely access for those who may benefit from disease-modifying therapy.

As one of the first European centers to implement anti-amyloid therapies in routine practice, CARD activated its dedicated programme in September 2024 and, as of 12 November 2025, has treated 32 patients (33 total prescriptions, including one switch from lecanemab to donanemab following insufficient biological response on 6-month follow-up amyloid PET). The pathway is supported by a multidisciplinary team including five attending neurologists, two neurology

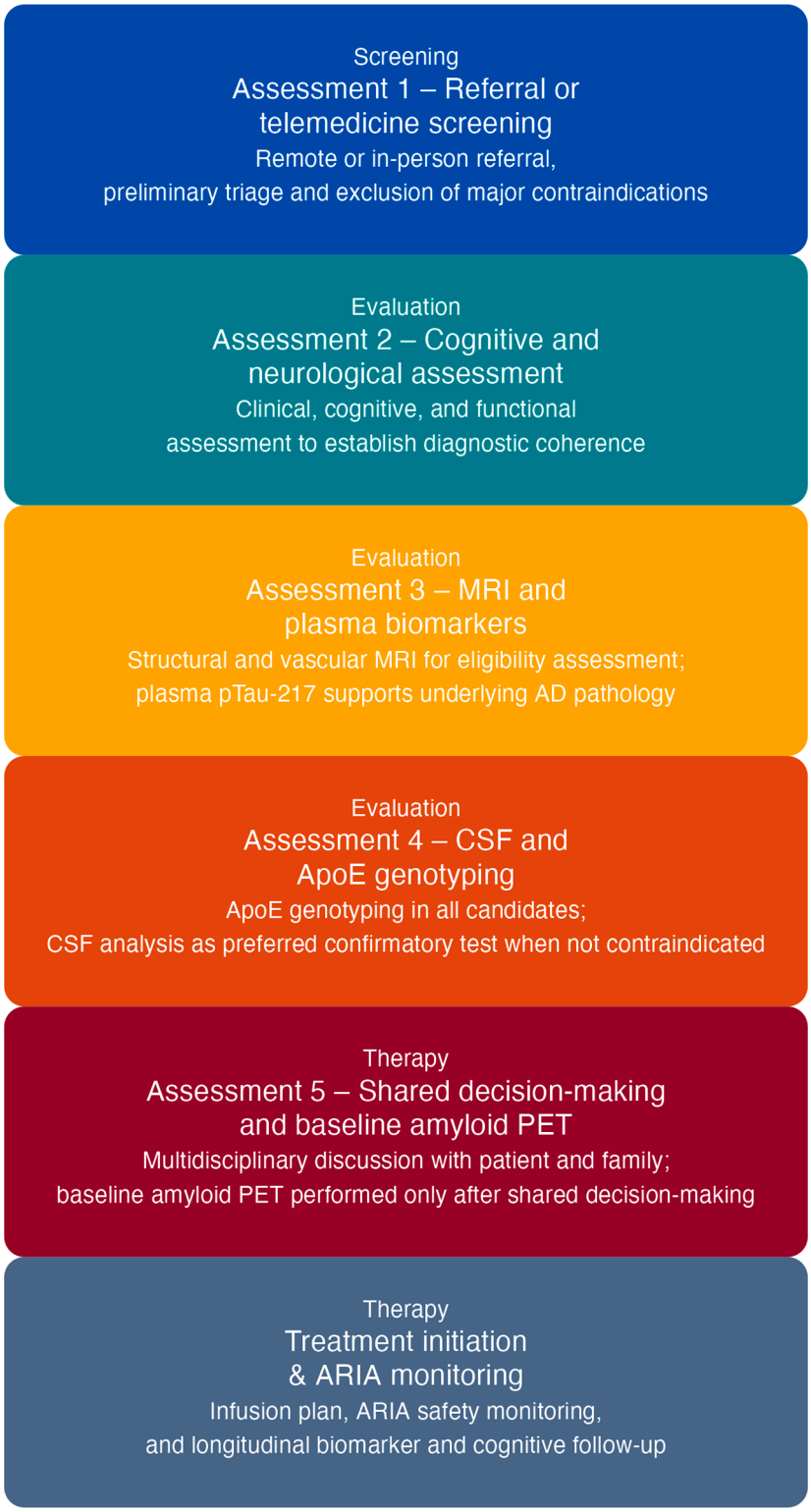

Fig. 1: **Patient journey for eligibility and initiation of anti-amyloid therapy**. A fast-track pathway designed to ensure timely assessment and treatment readiness in candidates for anti-amyloid monoclonal antibodies. Screening includes referral or telemedicine triage and exclusion of major contraindications. Clinical and functional assessment establishes diagnostic coherence, followed by MRI-based eligibility

residents, six neuropsychologists, three neuroradiologists, four nuclear medicine specialists, and a dedicated clinical coordinator, who together oversee screening, biological confirmation, MRI and ARIA surveillance, and infusion management.

Among treated patients, the mean age was 67.9 years (SD 7.9; range 55.3–83.0). Baseline cognitive measures were as follows: CDR global score mean 0.66 (SD 0.24; range 0.50–1.00), CDR-SB 3.27 (1.67; 1.00–7.00), MMSE 24.19 (3.82; 16–29), ADAS-Cog 17.42 (8.37; 5.99–42.33), and ADCS-MCI-ADL 41.13 (7.54; 18–52). Twelve patients are ApoE ε3/ε4 carriers and 20 are ε4 non-carriers; consistent with EMA recommendations, ApoE ε4/ε4 homozygotes and individuals on anticoagulants are excluded from treatment.[3,4] In this real-world setting, the mean time from initial screening to treatment initiation was 10.3 weeks (SD 5.0; range 3.9–27.1), underscoring the feasibility of an accelerated diagnostic–therapeutic pathway in a tertiary memory center. Importantly, this interval also encompasses the time required for patients and their families to consider and reach an informed decision, which may be longer than expected in the context of reimbursed therapies, given the out-of-pocket nature of the treatment.

Following treatment initiation, patients enter a structured biological and clinical follow-up program. In our center, amyloid PET imaging, plasma biomarker testing, and cognitive assessments are systematically repeated every 6 months to quantify amyloid clearance, monitor downstream biological changes, and evaluate cognitive–functional trajectories. This standardized schedule supports timely detection of treatment response and guides decisions regarding therapy continuation or adjustment.

Eligibility in routine practice: beyond trial-derived thresholds

Pivotal trials of anti-amyloid therapies have defined tightly selected, homogeneous populations. In routine practice, however, clinicians face a far wider spectrum of cognitive profiles, functional presentations, and biomarker constellations. In this context, rigid cognitive thresholds often fail to capture the patient's true disease stage or their potential to benefit from treatment.

Cognitive–functional discordance

A recurrent challenge is the imperfect correspondence between global cognitive scores and functional status. Some individuals with an MMSE below 20 may nonetheless preserve independence in daily activities and present a clinical picture aligned with stage 4 AD in the 2024 NIA–AA framework.[15] These discrepancies illustrate the limitations of fixed cutoffs when interpreted without clinical correlation.

Real-world evidence further supports the need for flexibility. In a recent U.S. implementation study, a patient presenting with a MoCA of 7 and an MMSE of 19 was re-evaluated three months later and scored 22 on the MMSE; functional assessment indicated mild dementia, and treatment with lecanemab was initiated despite the initially low MoCA score.[7] This example demonstrates that global scales cannot be interpreted in isolation and reinforce the importance of repeat testing, functional evaluation, and staging within a multidimensional framework.

Atypical AD phenotypes

These considerations must be distinguished from the challenges posed by atypical AD variants. Presentations such as primary progressive aphasia, posterior cortical atrophy, or dysexecutive–behavioral forms fall outside classic amnestic trajectories. Although underrepresented in trials, there is no mechanistic rationale to assume reduced efficacy or safety. Their younger age, relative preservation of functional capacity, and focal neuropsychological deficits often argue in favor of treatment when biomarker evidence is coherent.

Early-stage biomarker-positive individuals

At the opposite end of the clinical spectrum, we increasingly encounter individuals with biomarker-confirmed AD pathology but only subtle or subjective cognitive symptoms (stage 2 AD).[15] These patients are not eligible under current EMA indications, which restrict anti-amyloid therapy to mild cognitive impairment or mild dementia. Nevertheless, longitudinal observation frequently reveals measurable decline over follow-up, highlighting a therapeutic gap that future regulatory frameworks will need to address.[16,17]

MRI-based eligibility and hemorrhagic risk

MRI criteria introduce important real-world dilemmas. Current Appropriate Use Recommendations are based on GRE-derived thresholds for microbleeds and superficial siderosis, yet SWI (now widely used in clinical practice) detects a greater number of susceptibility lesions, many of uncertain clinical significance.[8,9,18] Automatic exclusion based solely on SWI-detected lesions risks denying treatment to otherwise suitable

evaluation and plasma pTau-217 testing to support underlying Alzheimer's pathology. ApoE genotyping is performed in all candidates, and CSF biomarkers are used as the preferred confirmatory test when feasible. Shared decision-making is completed before baseline amyloid PET. Treatment initiation includes infusion planning, ARIA safety monitoring, and longitudinal biomarker and cognitive follow-up. Abbreviations: MRI = magnetic resonance imaging; CSF = cerebrospinal fluid; ApoE = apolipoprotein E; ARIA = amyloid-related imaging abnormalities; PET = positron emission tomography.

candidates; in our practice, these findings are interpreted within a broader risk–benefit framework while awaiting harmonized guidance.

Standardized neuroradiology reporting, including harmonized sequences and structured documentation of microbleeds, siderosis, and vascular comorbidities, is essential for consistent and safe eligibility decisions. The presence of probable cerebral amyloid angiopathy (particularly when cortical superficial siderosis is identified) remains a major contraindication due to substantially increased hemorrhagic risk. Equally important is distinguishing ARIA-H, a treatment-related microhemorrhagic phenomenon, from spontaneous CAA-related hemorrhages, which have distinct mechanisms, prognoses, and implications for management.

Toward an individualized eligibility framework

Taken together, these examples highlight the need for integrative interpretation of cognitive, functional, imaging, and biological data to avoid inappropriate exclusion and to move toward individualized, clinically coherent eligibility decisions.

Safety monitoring and operational constraints

The advent of anti-amyloid therapies has redefined not only therapeutic goals but also the safety monitoring paradigm in AD. ARIA, particularly edema (ARIA-E) and microhemorrhages or superficial siderosis (ARIA-H), represent the most relevant safety concern, requiring structured MRI surveillance and close clinical oversight.[3,4,8,9,19] In pivotal trials, participants underwent serial MRI scans at baseline and at multiple timepoints during the first year, complemented by prompt imaging in case of neurological symptoms.[8,9]

Replicating these schedules in routine practice is challenging. MRI availability varies substantially across centers, and rigid timelines are often incompatible with clinical workflows, patient mobility, and comorbidities. Moreover, the requirement for frequent scans may increase patient burden and anxiety.

A risk-adapted surveillance model is emerging as a pragmatic alternative to universal high-frequency MRI. ApoE ε4 carriers, who have a significantly higher ARIA risk, may benefit from an intensified schedule, whereas ε3/ε3 individuals without baseline microbleeds may be safely monitored with fewer routine scans.[20,21] Such stratification reduces unnecessary imaging in low-risk patients while preserving safety in those at greatest risk.

Adjusting the titration scheme represents an additional pillar of ARIA risk mitigation. In TRAILBLAZER-ALZ 6 a slower dose-escalation of donanemab markedly reduced ARIA risk without attenuating amyloid removal or downstream biomarker response.[22,23] This regimen is now mandated by the EMA/CHMP label and therefore constitutes the standard dosing protocol across European centers. Our program had adopted this schedule even prior to formal regulatory approval, given its favorable safety profile, particularly in ApoE ε4 carriers. Early real-world observations confirm improved tolerability, with only mildly delayed amyloid clearance during initial cycles and convergence of biological efficacy over time.[24]

Operationally, urgent evaluation of neurological symptoms requires rapid access to MRI and specialist input. At our institution, a neurologist is available 24 h a day, 7 days a week, and radiology pathways allow for same-day MRI when ARIA is suspected. All treated individuals receive a bilingual Medical Alert Card detailing their ongoing therapy, the risk of ARIA, contraindications to anticoagulant and thrombolytic agents, and direct contact details for treating neurologists. This system ensures immediate recognition of therapy-related risk in emergency settings and facilitates rapid triage.

For many patients (especially those living outside our region) safety also depends on coordinated shared-care networks. Before treatment initiation, detailed monitoring schedules, ARIA management algorithms, and communication channels are shared with referring neurologists and local clinics. This collaboration enables prompt symptom assessment close to home while preserving consistency in management. Telemedicine further supports access, continuity, and rapid decision-making.

Together, these considerations illustrate that sustainable real-world implementation requires balancing rigorous trial-derived safety standards with practical constraints. A structured yet flexible safety architecture (combining risk-stratified MRI surveillance, genotype-informed titration, standardized emergency pathways, and shared-care networks) is essential to ensure safe and equitable delivery of anti-amyloid therapies across diverse healthcare systems.

Patient expectations and communication in the new era: navigating hope, uncertainty, and shared goals

The introduction of disease-modifying therapies has profoundly reshaped how AD is perceived by patients and families. A condition once regarded as an untreatable, age-related decline is now increasingly seen as a biologically defined disorder with modifiable trajectories.[15] This shift has generated a surge in early referrals, particularly among individuals in their 50s and 60s who are professionally active and often motivated by subtle symptoms, family history, or concerns about genetic risk. Young-onset patients commonly express fears related to heredity, employment, and long-term autonomy, placing communication at the center of clinical care.

Expectations frequently include hopes of symptom reversal or cure, requiring a clear reframing toward realistic goals: disease slowing rather than recovery of lost function, preservation of independence rather than full cognitive restoration. This tension between therapeutic hope and biological uncertainty must be addressed proactively, ensuring that optimism is balanced by transparency.

ApoE genotyping, now integral to risk stratification under EMA indications, plays a key role in these conversations. At our center, results are delivered directly by the treating neurologist, who contextualizes the implications for ARIA risk, treatment eligibility, and prognosis.

Shared decision-making extends well beyond treatment initiation. ARIA events, ambiguous benefit, comorbidities, or logistical burdens often require revisiting expectations and goals over time. A representative example from our practice illustrates these dynamics: a 61-year-old woman with MCI due to AD (ApoE ε3/ε3) developed multifocal moderate ARIA-E after her third donanemab infusion, presenting with transient vertigo and a brief fall. Treatment was paused, and monthly MRI follow-up showed complete resolution. Although AURs would allow re-initiation, the patient and her caregiver expressed concerns about cumulative risk. A re-challenge with delayed dose escalation was attempted, but a new mild, asymptomatic ARIA-E recurred after a single infusion. Following multidisciplinary discussion, treatment was discontinued, prioritizing safety and clinical stability over incremental benefit; follow-up amyloid PET will clarify the biological response. This vignette highlights the difficulty of sustaining a shared therapeutic purpose as clinical information evolves over time.

As disease-modifying therapies continue to diffuse into practice, communication itself becomes a core component of treatment. Sustained and evidence-based dialogue ensures that patients engage with these innovations as informed partners and that therapeutic decisions remain aligned with personal values, safety considerations, and the evolving scientific landscape.

Unresolved clinical questions

Despite the rapid adoption of anti-amyloid therapies, several key aspects of long-term management remain incompletely defined, and real-world practice is now shaping the next phase of therapeutic decision-making.

Treatment duration and stopping rules

Pivotal trials provide different paradigms: lecanemab was tested in a fixed-duration model with subsequent maintenance dosing, whereas donanemab adopts a treat-to-clear strategy in which dosing is discontinued once amyloid is substantially reduced on PET.[2–4,9] In clinical practice, however, boundaries are less clear. Should treatment continue indefinitely if amyloid PET remains low but cognition declines? How should clinicians define "lack of efficacy" in a condition that remains progressive even under therapy?

Available evidence suggests that amyloid reaccumulates slowly after discontinuation (on the order of 2–3 Centiloids per year) indicating that treatment effects may persist for several years.[25] These observations support the conceptual possibility of intermittent retreatment or re-initiation strategies, although formal validation of such approaches is still lacking.

Monitoring and biomarkers

While MRI is indispensable for ARIA surveillance, optimal long-term imaging strategies remain unsettled. The appropriate frequency and role of amyloid PET beyond initial clearance is also debated, particularly in treat-to-clear paradigms where the link between PET trajectories and clinical benefit is only beginning to be clarified.[26] The recently proposed treatment-related amyloid clearance (TRAC) framework introduces standardized categories of full and partial amyloid clearance based on quantitative PET, offering a common language to describe pharmacodynamic response and a conceptual basis for biomarker-informed monitoring.[26] However, TRAC currently relies primarily on serial amyloid PET, and its translation into routine practice (including integration with clinical outcomes and decisions about maintenance, discontinuation, or retreatment) remains an open research area.

Plasma biomarkers (pTau-217, pTau-181, Aβ42/40) are promising candidates for scalable monitoring and could eventually complement or reduce reliance on PET in TRAC-based algorithms, but no blood-based measure is yet validated to guide treatment duration, discontinuation, or switching decisions.[26] Establishing robust, biomarker-informed stopping rules is therefore a major unmet need.

Switching between different anti-amyloid antibodies

An emerging dilemma concerns the management of patients with suboptimal biological or clinical response. Current AURs allow switching from one monoclonal antibody to another after an adequate washout (typically ≥5 half-lives) to minimize overlapping pharmacodynamic effects and potential cumulative ARIA risk.[9] Early real-world data suggest that switching from lecanemab to donanemab can be feasible in carefully selected patients without prior ARIA, with no new safety signals during short-term follow-up.[27]

A case from our cohort illustrates this scenario. A 56-year-old woman with early-onset AD (ApoE ε3/ε3) completed six months of lecanemab with modest amyloid reduction (ΔCentiloid = 11) and measurable cognitive decline despite good adherence and absence of ARIA. After extensive shared decision-making, and following a washout corresponding to five lecanemab

***Fig. 2:* Key conceptual domains shaping the transformation of Alzheimer's care in the era of anti-amyloid therapy**. The introduction of disease-modifying anti-amyloid monoclonal antibodies requires a redefinition of diagnostic pathways, therapeutic eligibility, safety governance, organisational models, and ethical frameworks. Major elements include: (1) a shift from symptom-based to biologically anchored diagnosis supported by blood and imaging biomarkers; (2) translation of trial-based inclusion criteria into heterogeneous real-world populations; (3) adaptive ARIA risk management informed by ApoE genotype and MRI scheduling; (4) development of structured referral and monitoring networks integrating tertiary and local services; and (5) renewed attention to fairness, transparency, and shared decision-making as patient expectations evolve. Abbreviations: ApoE = apolipoprotein E; MRI = magnetic resonance imaging; ARIA = amyloid-related imaging abnormalities.

Search strategy and selection criteria

Searches were conducted in PubMed/MEDLINE and Embase to identify relevant literature on anti-amyloid monoclonal antibodies in Alzheimer's disease, with a focus on lecanemab, donanemab, disease-modifying therapies, amyloid-related imaging abnormalities (ARIA), and real-world implementation. We used a combination of MeSH terms and free-text keywords including "Alzheimer's disease", "anti-amyloid", "lecanemab", "donanemab", "amyloid PET", "plasma biomarkers", "ARIA", "real-world", and "clinical implementation". Reference lists of key articles, regulatory documents from the European Medicines Agency, and relevant consensus statements and appropriate use recommendations were also reviewed. We prioritised peer-reviewed articles, pivotal clinical trials, real-world observational studies, and authoritative guidelines published in English. Case reports, conference abstracts without full peer review, and studies not directly relevant to clinical implementation were excluded. This narrative review was not intended to be exhaustive, but to contextualise the authors' real-world experience within the available evidence.

half-lives, donanemab was initiated without safety complications.[9] This experience is consistent with the emerging TRAC-oriented paradigm, in which sequential therapy is considered in patients with limited amyloid clearance or ongoing decline despite adequate exposure.

Switching after ARIA raises more complex safety and communication challenges. Although not explicitly contraindicated, residual vascular vulnerability, patient preference, and the paucity of data often favour prolonged observation or definitive discontinuation rather than immediate re-challenge with the same or a different antibody. Until systematic evidence becomes available, such decisions must remain highly individualized and grounded in transparent discussion of uncertainty.

As real-world experience expands, therapeutic strategies are likely to evolve toward dynamic, biomarker-informed models that integrate clinical trajectory, ARIA risk, patient preferences, and biological endpoints (including TRAC status) rather than relying on rigid timelines. Multicenter registries and harmonized monitoring initiatives, such as those developed within the International Network for Real-world Alzheimer's Data (InRAD), will be essential to define evidence-based approaches for treatment duration, monitoring, and sequential therapy.[28]

Conclusion

The approval of anti-amyloid monoclonal antibodies marks a turning point in AD management, shifting from symptomatic relief to biological modification. Early real-world experience confirms feasibility but also reveals the complexity of applying trial-based protocols within diverse healthcare systems.

Three priorities emerge. First, timely and biologically anchored diagnosis is essential to avoid missing the narrow therapeutic window for treatment, underscoring the need for efficient referral pathways and equitable biomarker access. Second, monitoring must integrate both safety and efficacy. MRI remains indispensable for ARIA surveillance, but long-term management increasingly requires biological markers of response. Harmonized strategies are needed to guide continuation, discontinuation, or switching in routine practice. Third, clear communication and continuous shared decision-making are fundamental, particularly when expectations of improvement coexist with biological uncertainty or when treatment benefit becomes ambiguous. Together, these elements outline a multidimensional transformation of Alzheimer's care, integrating diagnostic, therapeutic, organizational, and ethical challenges (Fig. 2).

Looking ahead, sustainable implementation in Europe will depend on coordinated policies, equitable resource allocation, and robust real-world registries capable of translating a scientific breakthrough into a scalable, resilient, and patient-centered model of dementia care.

Contributors

MF, GC, and FA conceived the manuscript and defined its conceptual framework. MF, GC, and FA wrote the original draft of the manuscript. EGS, AG, GR, SP, and EC contributed to critical revision of the manuscript for important intellectual content. All authors reviewed and approved the final version of the manuscript.

Declaration of interests

MF is Editor-in-Chief of the *Journal of Neurology*, Associate Editor of *Human Brain Mapping*, *Neurological Sciences*, and *Radiology*; received compensation for consulting services from Almirall, Biogen, Bristol-Myers Squibb, Eli Lilly, Merck, Novartis, Roche, Sanofi; speaking activities from Amgen, Bayer, Biogen, Bristol-Myers Squibb, Celgene, Chiesi Italia SpA, Eisai, Eli Lilly, Fujirebio, Genzyme, Janssen, Merck, Neopharmed Gentili, Neuraxpharm, Novartis, Novo Nordisk, Roche, Sanofi, Takeda; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Eli Lilly, GE Healthcare Ltd, Merck, Neuraxpharm, Novartis, Roche, Sandoz, Sanofi, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and Fondazione Italiana Sclerosi Multipla. GC has received speaker honoraria from Neopharmed Gentili and Eli Lilly. EGS has nothing to disclose. AG has received speaker honoraria from Eli Lilly. GR has nothing to disclose. SP has nothing to disclose. EC has nothing to disclose. FA is Associate Editor of *NeuroImage: Clinical*, has received speaker honoraria from Biogen Idec, Roche, Eli Lilly, GE Healthcare and Bristol Myers Squibb, and receives or has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, AriSLA (Fondazione Italiana di Ricerca per la SLA), the European Research Council (ERC), the EU Joint Programme – Neurodegenerative Disease Research (JPND), and Foundation Research on Alzheimer Disease (France).

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