Devenir leader européen en recherche clinique: nos propositions

Enquête « attractivité de la France pour la recherche clinique » - 13ème édition

Executive Summary

Enquête « Attractivité de la France en recherche clinique »

Essais industriels sur le médicament initiés entre le 1er janvier 2022 et le 30 juin 2023. Analyse de la compétition internationale (base Trialtrove) et des résultats français (base Oscar) et identification des bonnes pratiques espagnoles

Les entreprises du médicament, engagées en faveur de la recherche clinique

- Premier accès à l'innovation pour les patients, promotrices de la majorité des essais thérapeutiques
- Partenaires de l'ensemble des acteurs de la recherche clinique sur le territoire
- Investissement dans des développements innovants

L'ambition de leader en Europe, portée par France 2030, menacée par une forte compétition internationale

- US en tête dans les domaines de recherche les plus dynamiques et changements règlementaires EU peu attractifs
- France en 3ème position en EU
- Espagne continue à creuser l'écart face à l'Allemagne, la France, le Royaume-Uni et l'Italie

Plan d'actions du Leem

Objectifs des entreprises: augmenter la participation de la France aux essais internationaux (+25%), contribuer au démarrage des essais en 120 jours

Principes collectifs: l'engagement de l'ensemble des acteurs, l'intégration des essais au parcours de soins, le co-pilotage public-privé des actions

Actions prioritaires en 2024:

- Supprimer l'autorisation d'exportation-importation des échantillons biologiques pour démarrer un essai
- Simplifier la convention unique & mettre en place un fast track « démarrage en 120 jours » sur les essais innovants
- Intégrer la décentralisation et la digitalisation dans la recherche clinique

leem

Les entreprises du médicament engagées pour la recherche clinique en France

→ *elles sont promotrices de la majorité des essais sur le médicament*

684 essais initiés en France par les entreprises

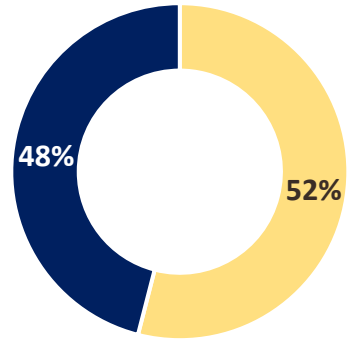
72% des essais autorisés

224 entreprises du médicament promotrices

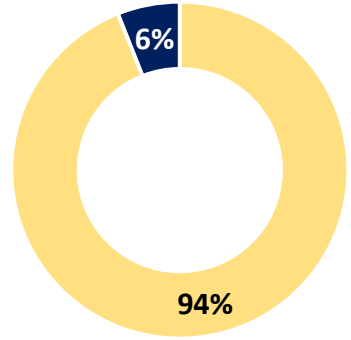
52% de ces essais sont promus par le Top20* pharma

94% des essais ont une dimension internationale

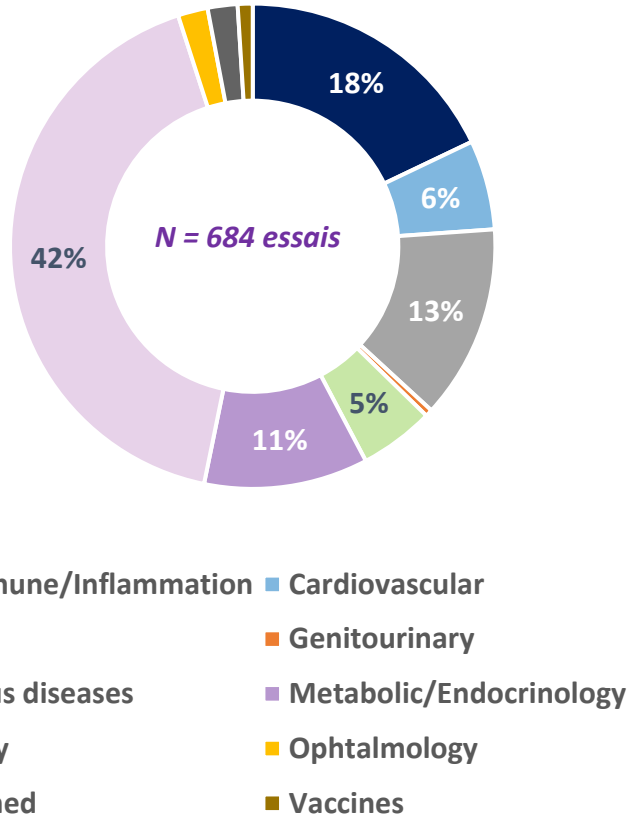
*basé sur le chiffre d'affaires mondial



n=684 essais Initiés entre le 1er janvier 2022 et le 30 juin 2023



Les essais cliniques apportent un 1er accès à l'innovation aux patients



Des essais pour les patients atteints:

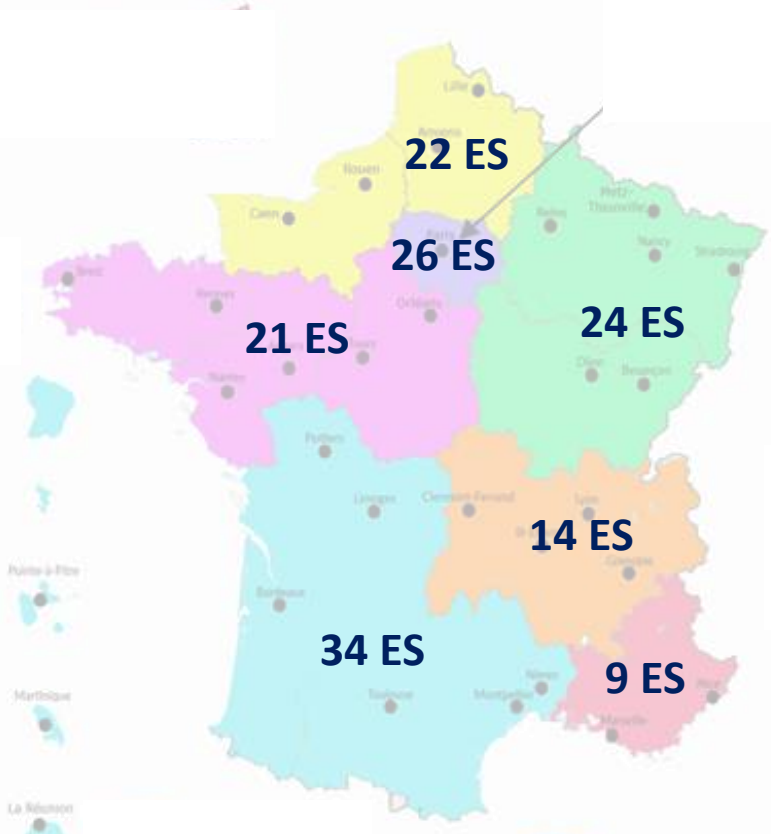
- de cancers (42%)
- de maladies auto-immunes (18%)
- de maladies du système nerveux central (13%)

Au niveau européen, la France participe à :

49% des phases précoces en cancérologie
50% des essais sur les cancers rares
43% des essais sur les maladies rares
43% des essais pédiatriques

Les entreprises du médicament sont des partenaires de l'ensemble des acteurs de la recherche clinique en France

Nombre d'établissements de santé (ES) partenaires par inter-région



- **684 essais industriels ont été initiés sur le territoire avec 150 établissements de santé: CHU, CH, CLCC, EBNL, clinique, SSA***
- **112 essais académiques (hospitaliers, associatifs ou de groupes coopérateurs) ont été soutenus par les entreprises du médicament**

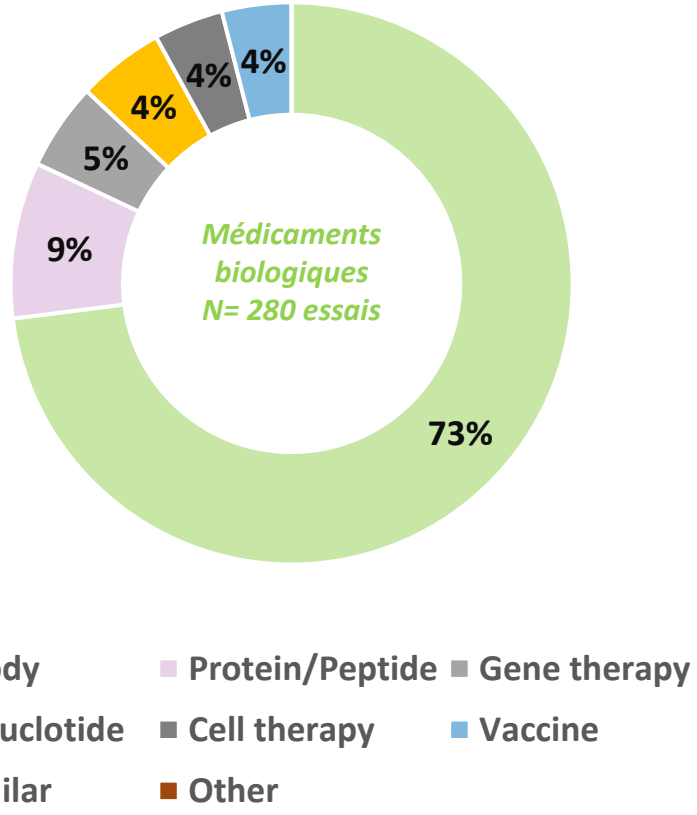
*Centre Hospitalier Universitaire, Centre Hospitalier, Centre de Lutte Contre le Cancer, Etablissement à But Non Lucratif, Clinique, Service de Santé des Armées

Les entreprises du médicament investissent dans des développements cliniques innovants

41% des essais évaluent des médicaments biologiques
- dont 73% sont des anticorps,
- 9% sont des protéines ou des peptides
- et 9% sont des thérapies géniques ou cellulaires

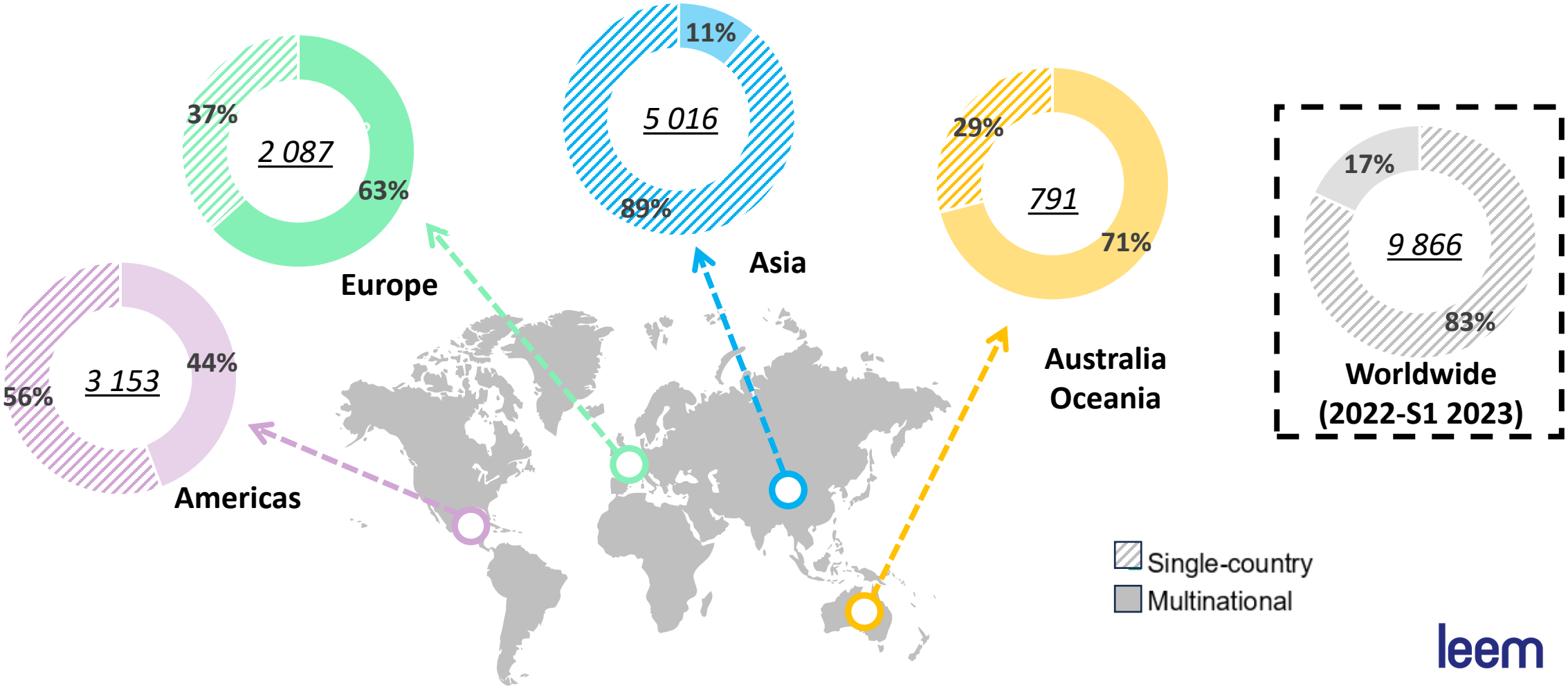
77% des essais utilisent des biomarqueurs

13% présentent une approche innovante (design, méthodologie, décentralisation)



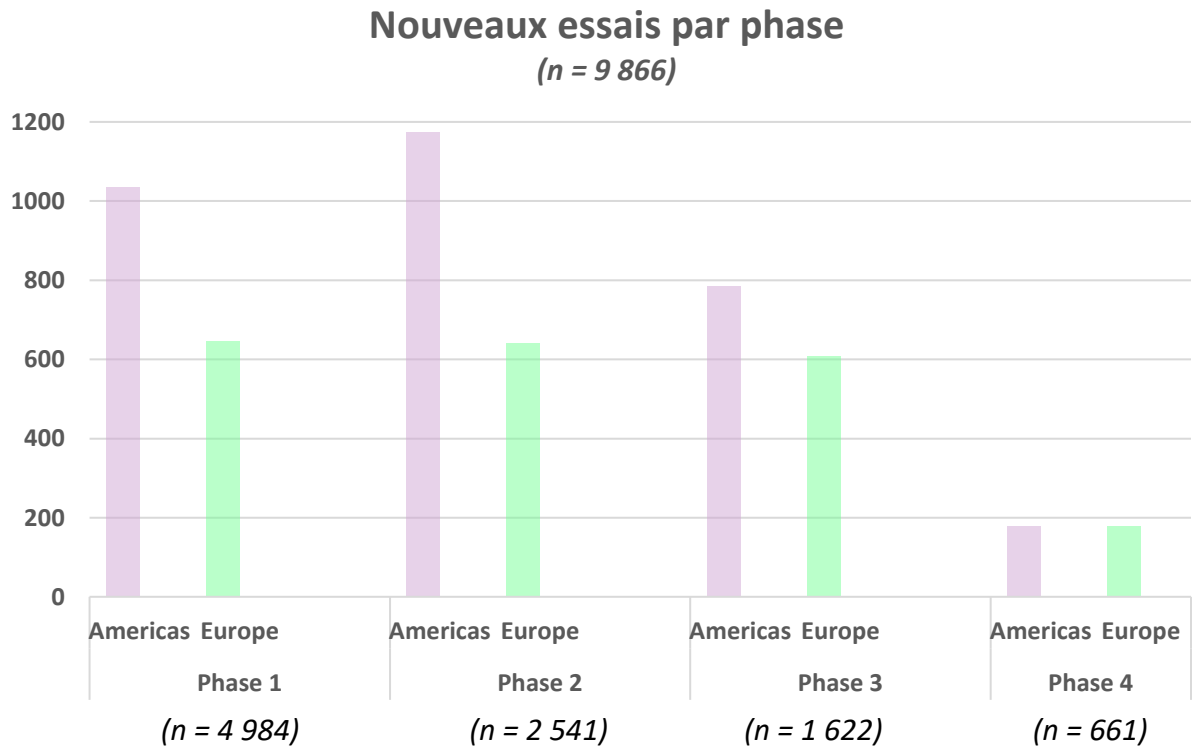
L'Europe est en compétition avec d'autres grandes régions

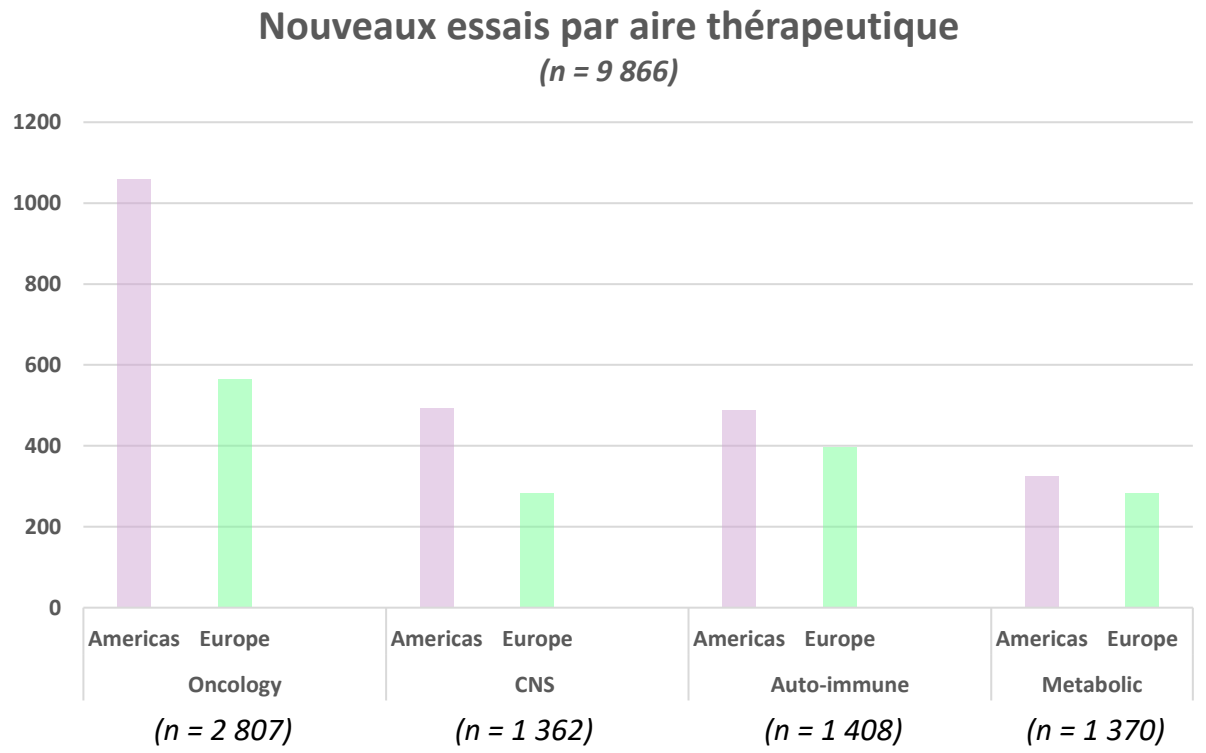
→ *l'Europe est positionnée au 3ème rang mondial et au 2ème rang pour les essais multinationaux*



Pour les domaines les plus dynamiques, l'Europe est devancée par le territoire américain

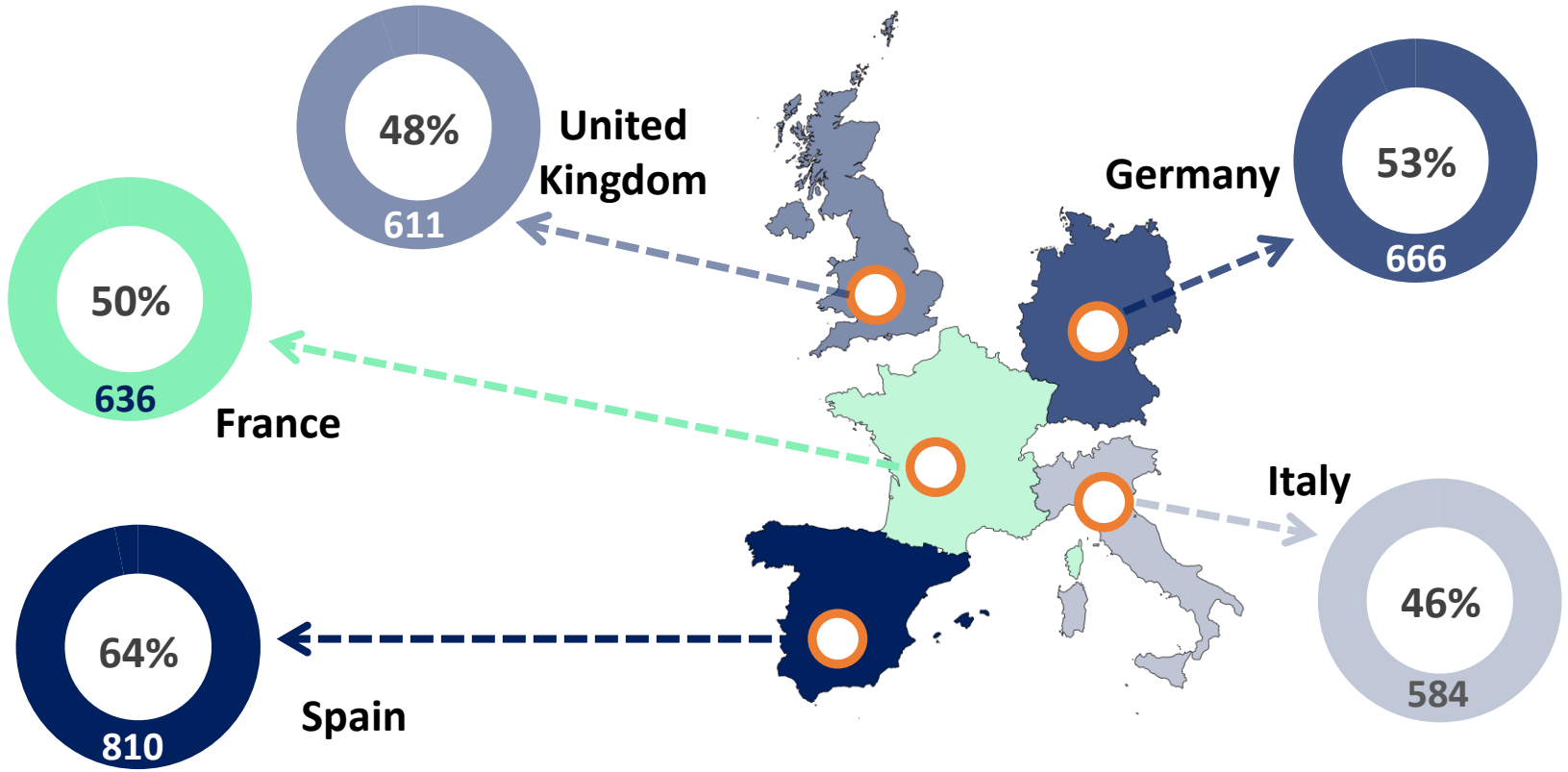
→ *sur les phases 1 & 2 (76% des essais)*
→ *en cancérologie (28%), maladies du SNC (14%), métaboliques (14%) , auto immunes (14%)*





L'Espagne continue à se distinguer et la France maintient son 3ème rang en EU

➔ *La France participe à la moitié des essais initiés sur le territoire européen*



100%
1261

Europe

Essais multinationaux hors volontaires sains (2022 – S1 2023)

Une situation menacée avec une attractivité de la France challengée

→ *la France conserve son 2ème rang européen en cancérologie mais est talonnée par l'Allemagne et le Royaume-Uni pour les phases 1&2*

% Europe (n trials)	*Phase 1*	*Phase 2*	*Phase 3*	*Phase 4*
France	**37% (57)**	**47% (238)**	59% (303)	46% (37)
Germany	32% (50)	46% (234)	65% (334)	**58% (46)**
Italy	25% (38)	41% (208)	60% (308)	36% (29)
Spain	**58% (89)**	**61% (310)**	**73% (375)**	44% (35)
United Kingdom	31% (47)	46% (235)	57% (291)	45% (36)
Europe	100% (154)	100% (510)	100% (514)	100% (80)

Oncology	*CNS*	*Auto-immune*	*Metabolic*
60% (263)	52% (85)	27% (119)	45% (62)
48% (212)	56% (90)	**38% (168)**	**52% (72)**
49% (217)	59% (95)	24% (107)	47% (66)
75% (332)	**61% (99)**	35% (156)	45% (62)
48% (211)	54% (88)	28% (122)	49% (68)
100% (442)	100% (162)	100% (265)	100% (139)

Essais multinationaux hors volontaires sains

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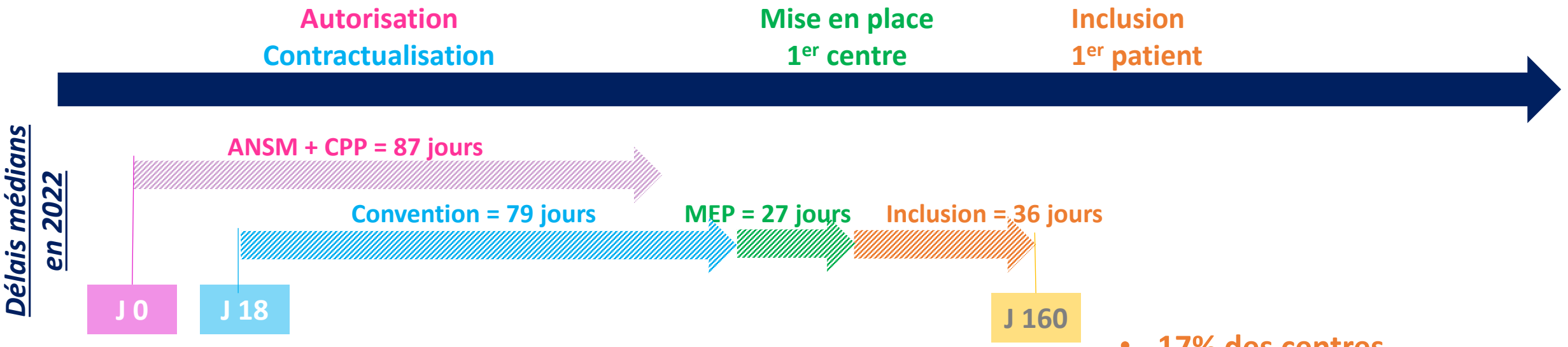
En 2022, 160 jours étaient nécessaires pour inclure un 1er patient en France

→ *les délais de démarrage doivent désormais composer avec les Règlements européens (CTR & IVDR) et les performances d'inclusion restent perfectibles*



- **17% des centres investigateurs sans inclusion**
- **86% des objectifs d'inclusion atteints**

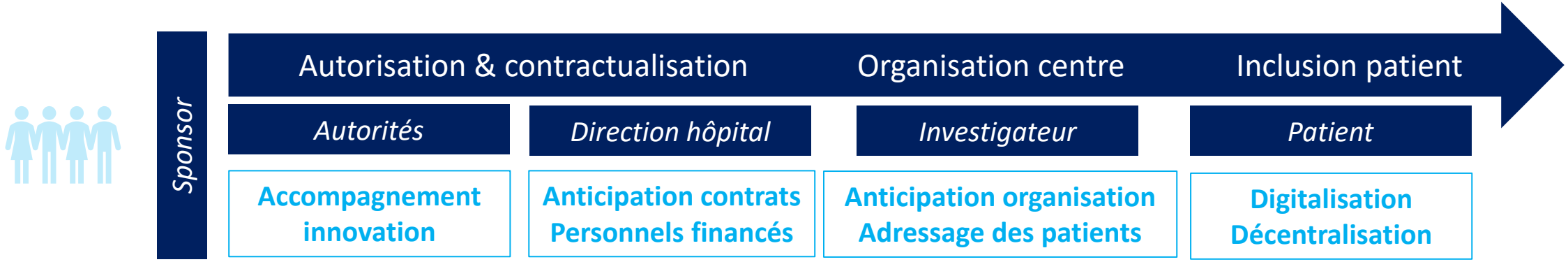
Identification des bonnes pratiques espagnoles

Trois étapes 2015-2022

- 1er pour phases précoces cancer
- 1er pour toute la cancérologie
- 1er ou 2ème pour autres aires

Performance opérationnelle

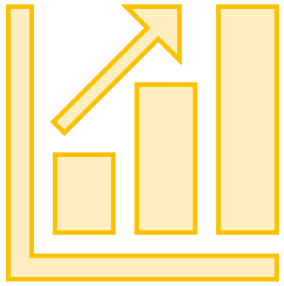
- Autorisation en 53 jours depuis 2016
- Contractualisation en 60 jours pour phases précoces & cancer depuis 2019
- Taux d'inclusion dans les centres de 94%



Devenir *leader* européen en recherche clinique

Principes collectifs

- Engagement des acteurs
- Recherche clinique intégrée au parcours de soins
- Co-pilotage public – privé



Objectifs des entreprises

- Augmenter la participation de la France aux essais multinationaux (+25%)
- Accélérer le démarrage des essais (120 jours)

Autorisation & contractualisation → Organisation centre → Inclusion patient

Supprimer l'autorisation d'exportation/ importation des échantillons biologiques

Simplifier la convention unique (forfait par visite) et mettre en place un *fast track « démarrage en 120 jours »* pour les essais innovants

Intégrer la décentralisation aux essais cliniques & pérenniser la plateforme nationale ECLAIRE

Garantir la présence de personnels formés au sein des structures dédiées à la recherche
Co-piloter collectivement la performance de la France en recherche clinique en s'appuyant sur un outil de recueil et de suivi des indicateurs

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Attractivité de la France pour la recherche clinique

Focus cancérologie & phases précoces

Rencontre 2023 de phases précoces
en cancérologie – 30 novembre 2023

Executive Summary

Enquête « Attractivité de la France en recherche clinique » - focus cancérologie

Essais industriels sur le médicament initiés entre le 1er janvier 2022 et le 30 juin 2023. Analyse de la compétition internationale (base Trialtrove) et des résultats français (base Oscar) avec un focus cancérologie et phases précoces

La cancérologie est le « driver » de l'innovation et concerne 30% des essais initiés dans le monde

- Amérique – Europe – Asie : trio pour les essais multinationaux en cancérologie
- Enjeu européen: préserver cette attractivité malgré les changements réglementaires (CTR, IVDR)
- Pour les phases précoces: limiter les stratégies d'évitement de la région UE (vers Corée du Sud, UK, Canada, Australie)

La France au 2ème rang européen en cancérologie et pour les phases précoces en cancérologie

- La France participe à 60% des essais européens en cancérologie (versus 75% pour l'Espagne)
- La France participe à 49% des essais européens de phases précoces en cancérologie (versus 67% pour l'Espagne)
- Phases précoces = levier unique d'attractivité en cancérologie pour la France (autres pays du Top 5 EU étant très présents et efficients pour les phases III
- La France dispose d'un réservoir européen de 180 essais en cancérologie (dont 89 phases précoces)

Plan d'actions du Leem

- Garantir *continuum* entre le développement clinique (phases précoces, essais d'enregistrement) et l'accès à l'innovation (accès dérogatoire et droit commun)
- S'engager collectivement sur des *fast tracks* « démarrage en 120 jour » pour les étapes
  - autorisation (cellule phase précoce, articulation CTR/IVDR)
  - contractualisation (fluide, échange privilégié en parallèle de l'autorisation)
  - inclusion (anticipation et organisation des centres investigateurs par les sponsors)

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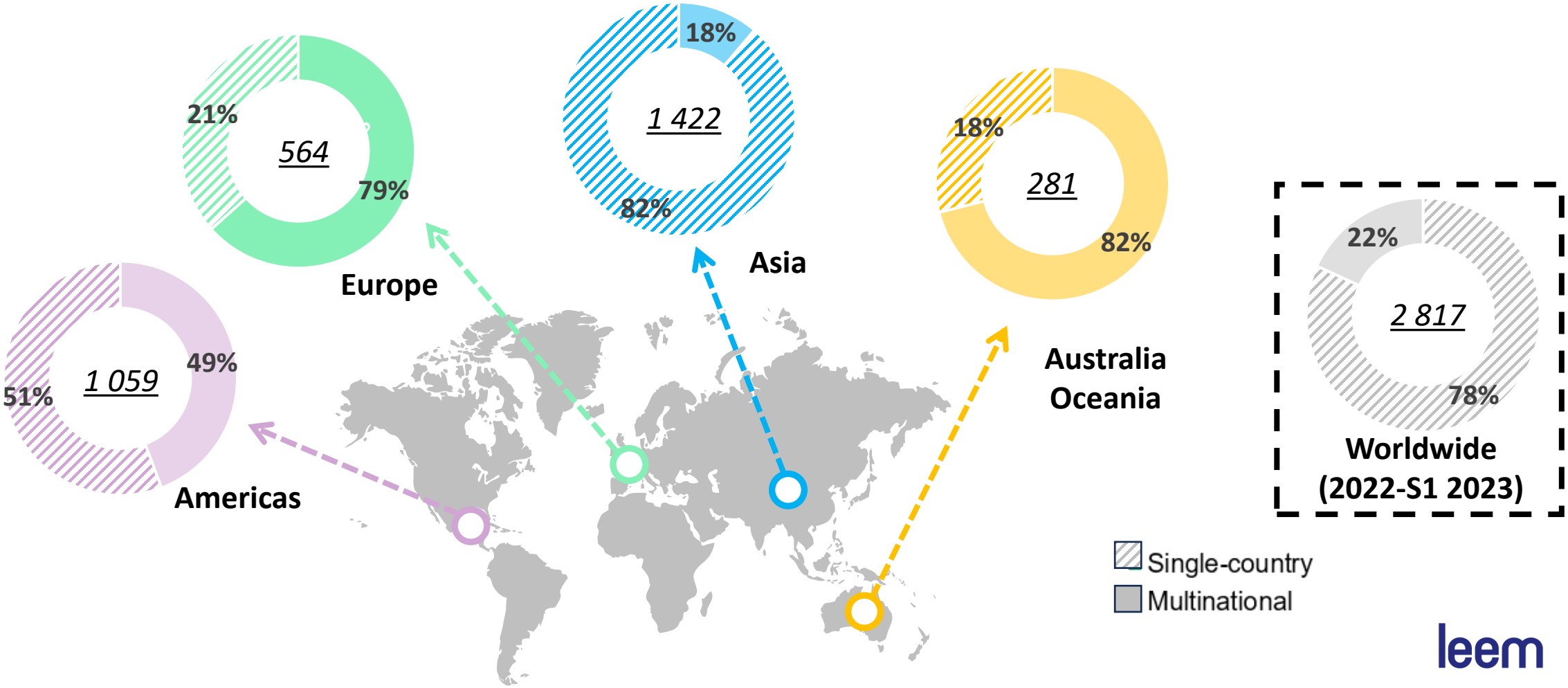
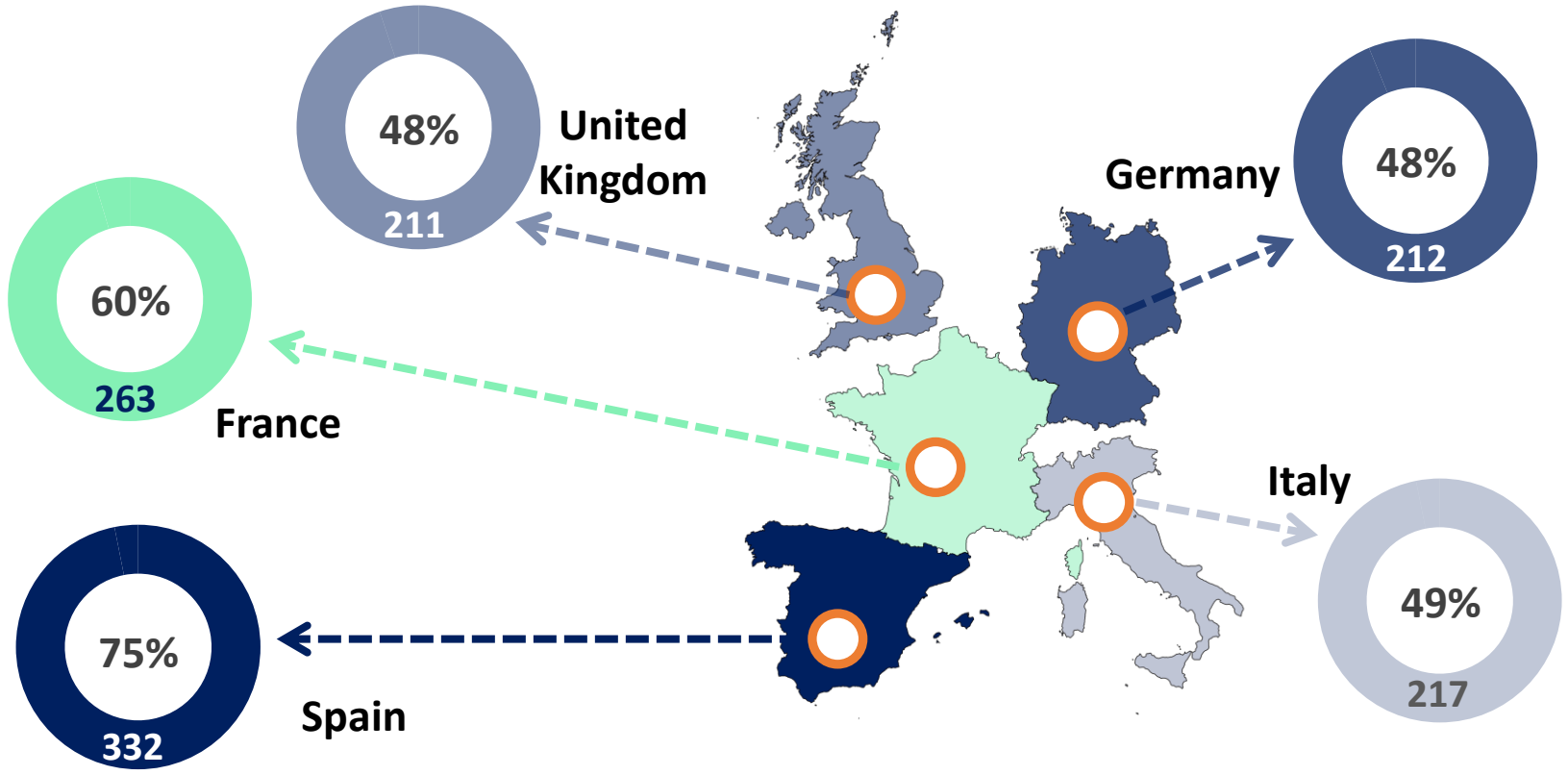
L'Europe participe à 73% des nouveaux essais multinationaux en cancérologie

→ *l'Europe est positionnée au 3ème rang mondial et au 2ème rang pour les essais multinationaux*



La France confirme son 2ème rang dans la compétition européenne pour les essais industriels multinationaux en cancérologie



100%
443

Europe

Essais multinationaux hors volontaires sains (2022 – S1 2023)

Un 2ème rang pour la France dans la compétition européenne en cancérologie y compris pour les phases précoces

175 nouveaux essais de phases précoces en oncologie en Europe (2022-S1 2023)

49% promus par le Top 20 pharma

6% des essais accessibles à la pédiatrie

6% des essais thérapie génique / cellulaire

% Europe (n trials)	*Oncology Phases 1 et 1/2*	*Oncology Phase 2*	*Oncology Phase 3*
France	**49% (86)**	**60% (85)**	**75% (85)**
Germany	31% (54)	46% (65)	74% (84)
Italy	31% (54)	55% (78)	71% (81)
Spain	**67% (117)**	**79% (111)**	**85% (97)**
United Kingdom	37% (65)	44% (62)	68% (77)
Europe	100% (175)	100% (141)	100% (114)

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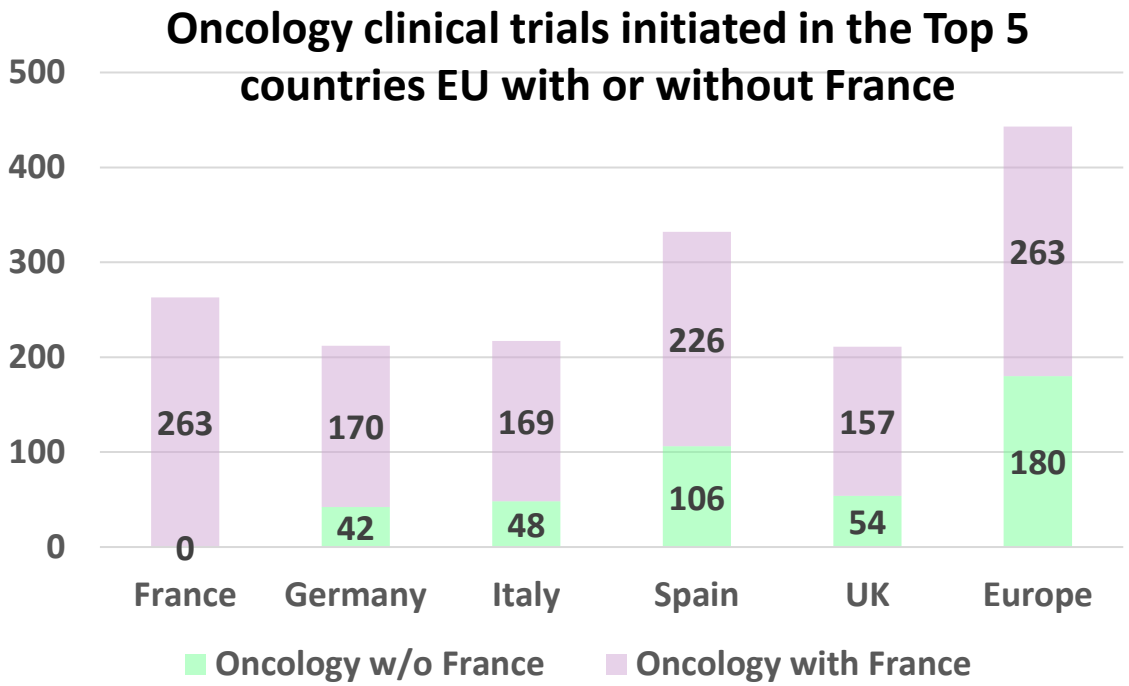
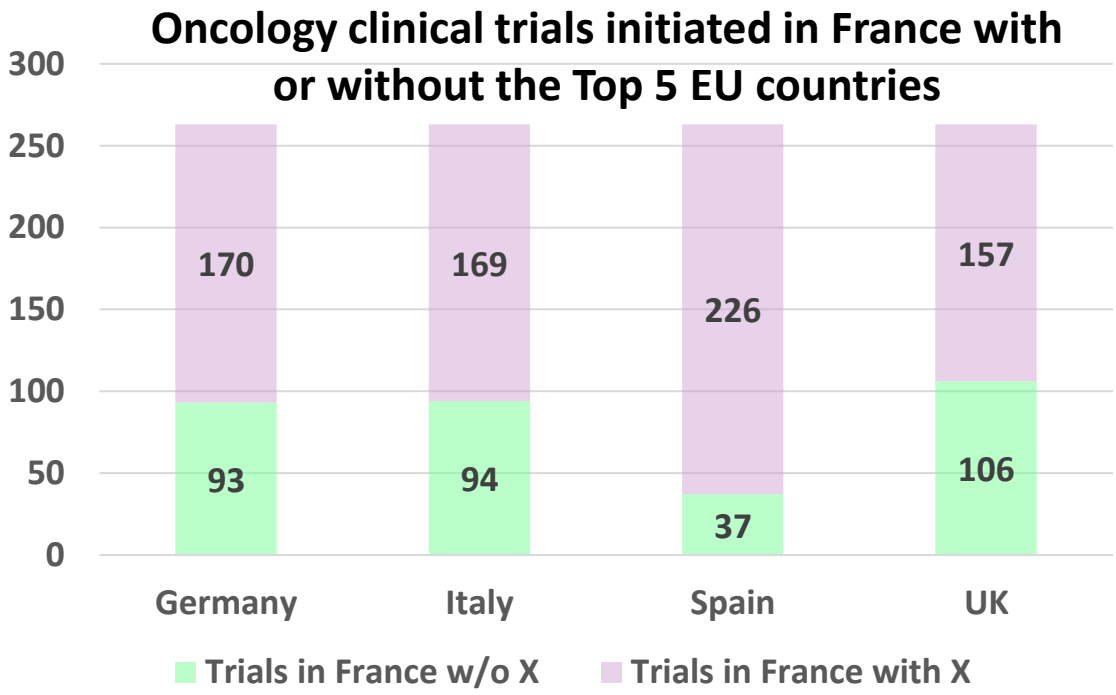
La France dispose néanmoins d'un réservoir de 180 essais industriels multinationaux en cancérologie dont 89 essais de phases précoces

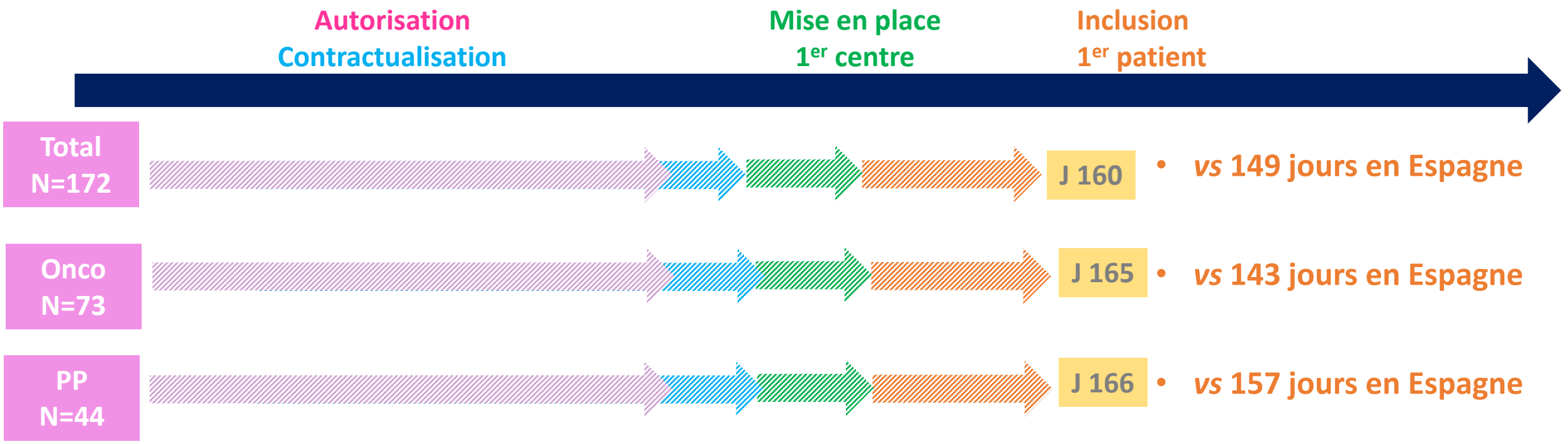




86 essais promus par le Top 20 pharma (sur chiffre d'affaires mondial)

94 essais promus par 81 autres entreprises du médicament

En 2022, 165 jours étaient nécessaires pour inclure un 1er patient en France dans un essai de cancérologie versus 143 jours en Espagne



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Attractivité de la France pour la recherche clinique

Focus sur la compétition internationale

Analyse de la base TRIALTROVE

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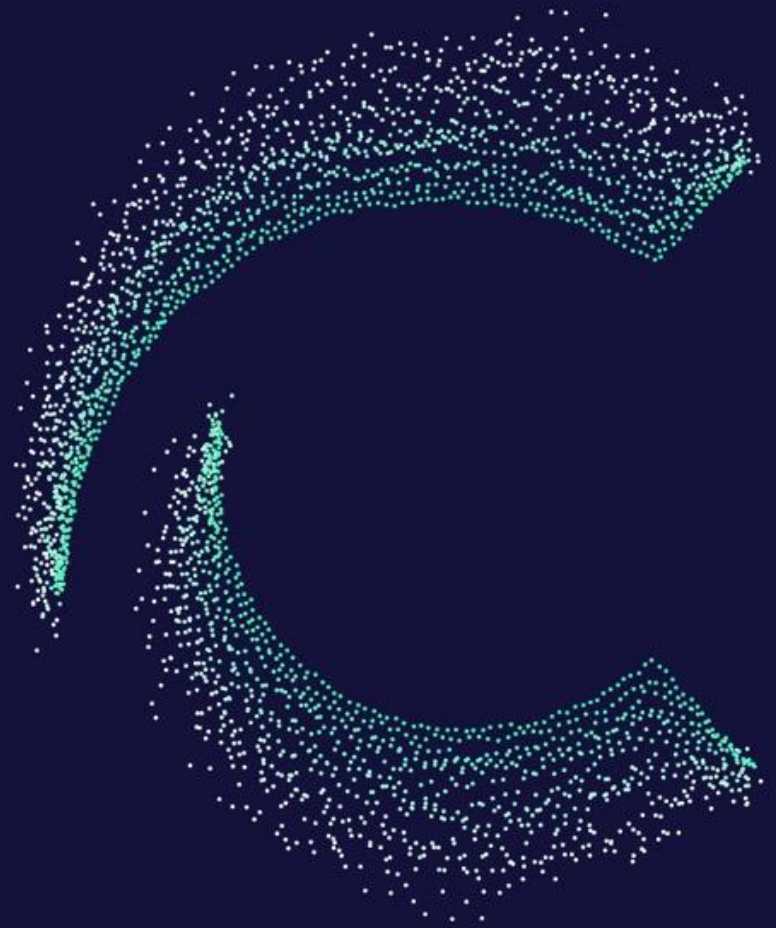
Clinical Research Attractiveness

leem
les entreprises du médicament

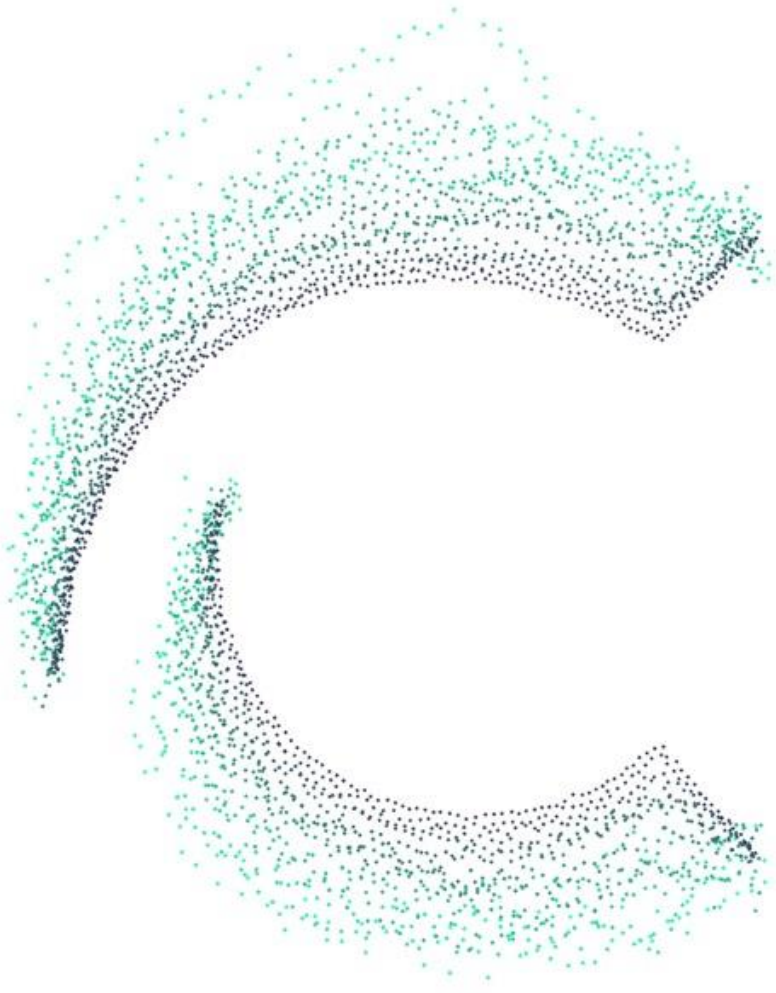


Prepared by Citeline | Evaluate Consulting & Analytics

2nd November 2023

CITELINE

1. Objectives & Methodology



Project Objectives and Scope

LEEM requires an analysis of ongoing Clinical Trials in France to understand where France's strengths and areas of focus lie in clinical research; comparisons to made across Europe, and between continents

LEEM's Objectives

- Characterise and segment clinical research promoted by drug companies in France
- Compare recent trials to previous studies and identify trends
- Understand where France places among international competition and European competitors
- Appraise France's strengths and areas of excellence
- Highlight areas of progress
- Gain an understanding of innovation in clinical trials

Scope

- The analysis will be conducted on a dataset of trials conforming to the following criteria:
  - Interventional studies of a pharmacologically active therapy, cell therapy, or gene therapy
  - Industrial sponsorship (whether with or without academic collaboration)
  - Start date from 1/1/2022 to 30/6/2023
- The analyses will be conducted at two geographic levels:
  - A high-level overview of comparisons between continents
  - A detailed comparison of France compared with the four other major European markets (Germany, Spain, Italy, UK) and compared with European average

Methodology / Terminology

Citeline | Evaluate has used Trialtrove to identify the pre-defined set of relevant Clinical Trials; Pharmaprojects and Scrip have been utilized for additional analyses

Sources

TRIALTROVE
CITELINE CLINICAL

PHARMAPROJECTS
CITELINE CLINICAL

SCRIP
CITELINE COMMERCIAL

Clinical Trials

- **Clinical Trials are the foundational entities counted in this analysis**
- A trial may have sites in >1 country and >1 continent
- Multinational trials have sites in >1 country
- Single-country trials have sites in only 1 country (though may have multiple sites in that country)
- A trial may have >1 sponsor and >1 sponsor type
- A trial may be investigating >1 therapeutic intervention and therefore may count towards more than one modality category
- A trial may contribute to > 1 disease and > 1 therapy area

Territories

- Western Asia/Middle East is considered a distinct continent and does not contribute to the counts for Asia
- Europe refers to the whole continent and is not limited to the EU.
- Within the analyses in the European Focus section, a single clinical trial may contribute to the counts for more than one of the EU4+UK comparator countries. However, within the Europe category on those charts, each trial is counted only once

Therapeutic Area

- The unassigned therapeutic area is populated by trials that do not align with any of the 9 other listed therapeutic areas

Trial Phase

- Trials are segmented by phase throughout the deck into either Phase 1, Phase 2, Phase 3, or Phase 4 trials
- Phase 1/2 trials are rolled into the Phase 2 category; Phase 2/3 trials are rolled into the Phase 3 category, and Phase 3/4 trials are rolled into the Phase 4 category
- "Other" is assigned to studies that cannot be clearly aligned with any of the main phases. These include trials that do not include typical safety/efficacy clinical endpoints such as response rate or progression-free survival, and which have not been assigned a specific phase by the sponsor. These trials usually do not have FDA- or EMEA-accepted surrogate endpoints, but rather look at biomarkers, pharmacogenetics, pharmacogenomics, and other disease-related endpoints that may be mechanistic in nature.

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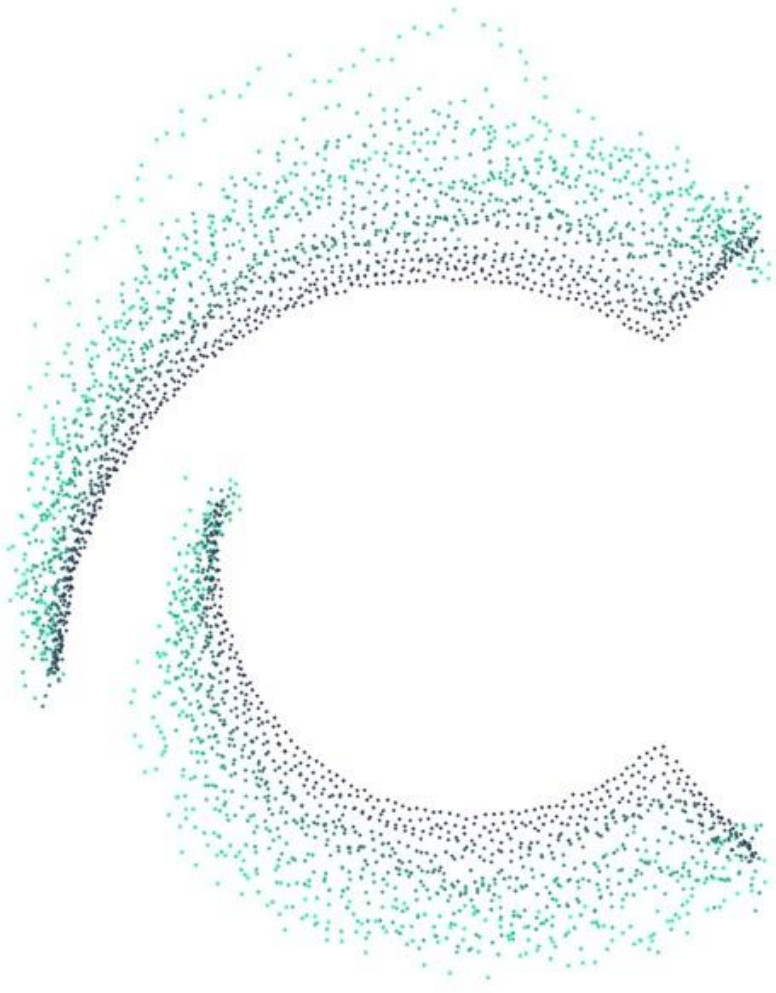
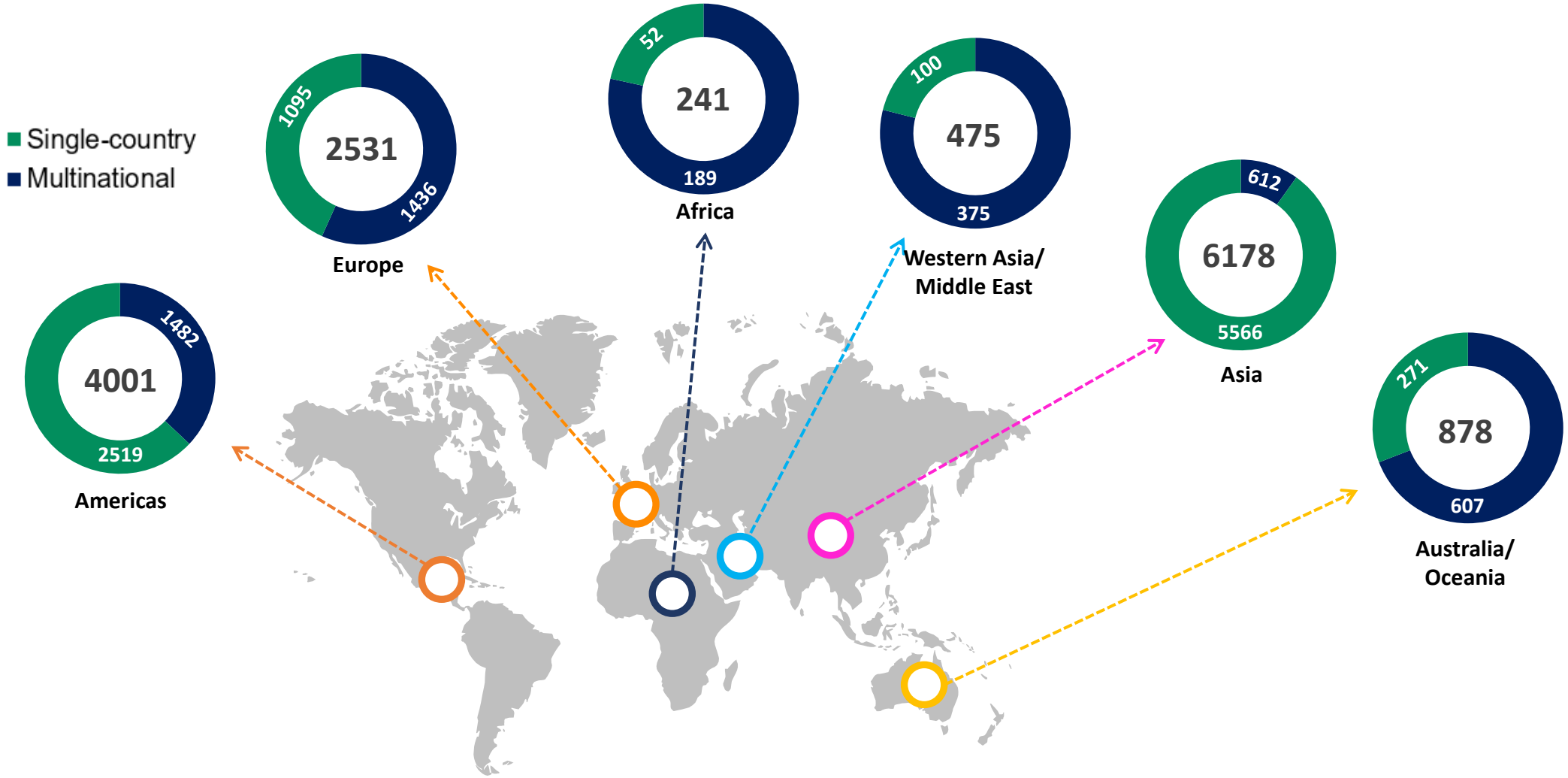
2. Continental comparison



Multinational vs Single-Country Trials (2022 and S1-2023, industry and non-industry co-sponsors trials)

Europe has a greater ratio of multinational vs single-country trials than Asia or the Americas; Asia has the highest proportion of single-country trials among all continents

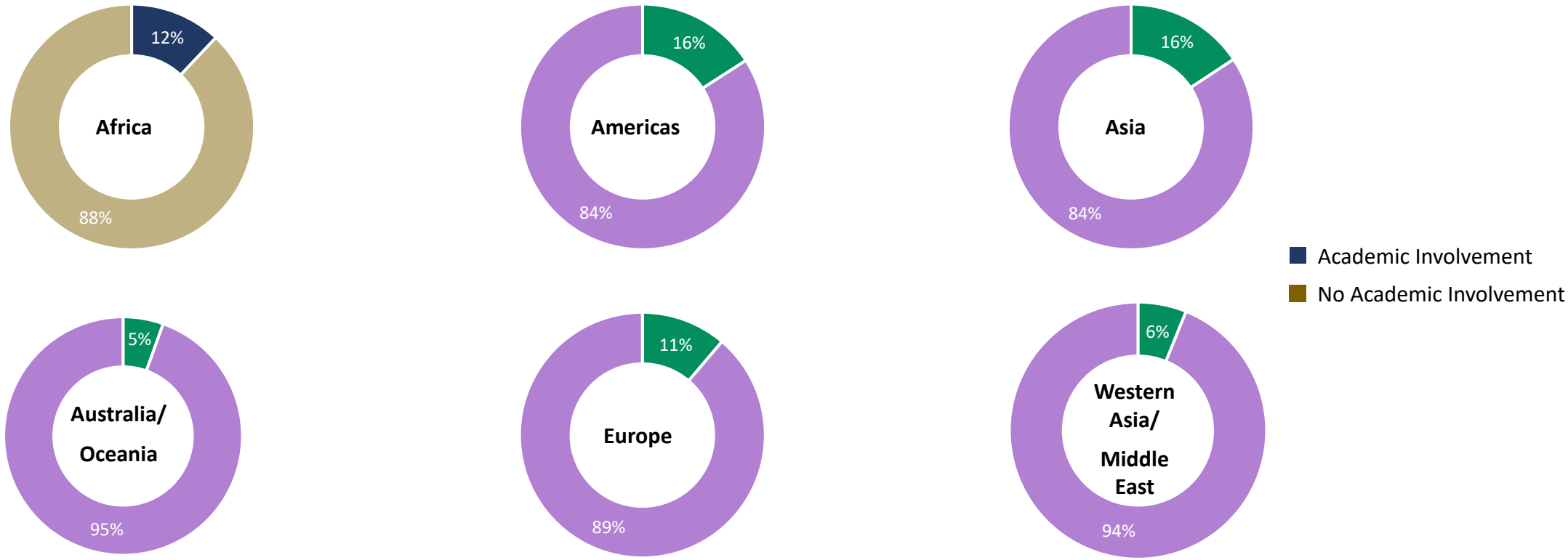


Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; Trials may have a non-industry co-sponsor. A single multinational trial may have sites in >1 continent and may contribute to the counts for multiple continents; Western Asia / Middle East is here considered a distinct continent and not included in the count for Asia;

Proportion of Trials with Academic Collaboration

A comparable percentage of trials have academic involvement across Europe, Africa, Asia, and the Americas; trials in Oceania and trials in the Western Asia/Middle East have the lowest extent of academic involvement

Percentage of Trials with an Academic Collaborator (In Addition to an Industrial Sponsor) (2022–2023)

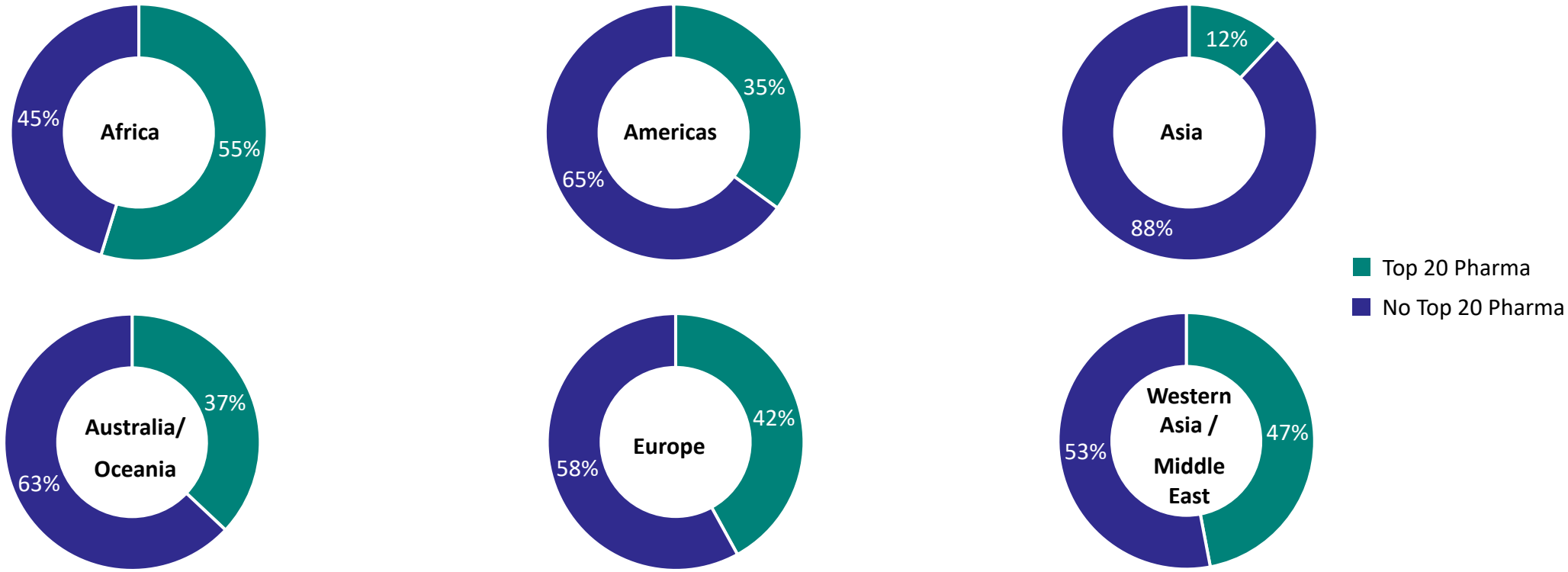


Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 continent and may contribute to the counts for multiple continents; Western Asia/ Middle East is here considered a distinct continent and not included in the count for Asia; Academic institutions, as per Citeline Trialtrove, include institutions affiliated with a university or whose medical operations also involve an academic aim. This includes teaching hospitals, university hospitals, and research institutes that are not administered by government entities

Proportion of Trials with Top 20 Pharma Involvement

Africa is the only continent in which Top 20 Pharma are involved in >50% of all clinical trials; the absence of Top 20 Pharma companies is most pronounced among studies taking place in Asia

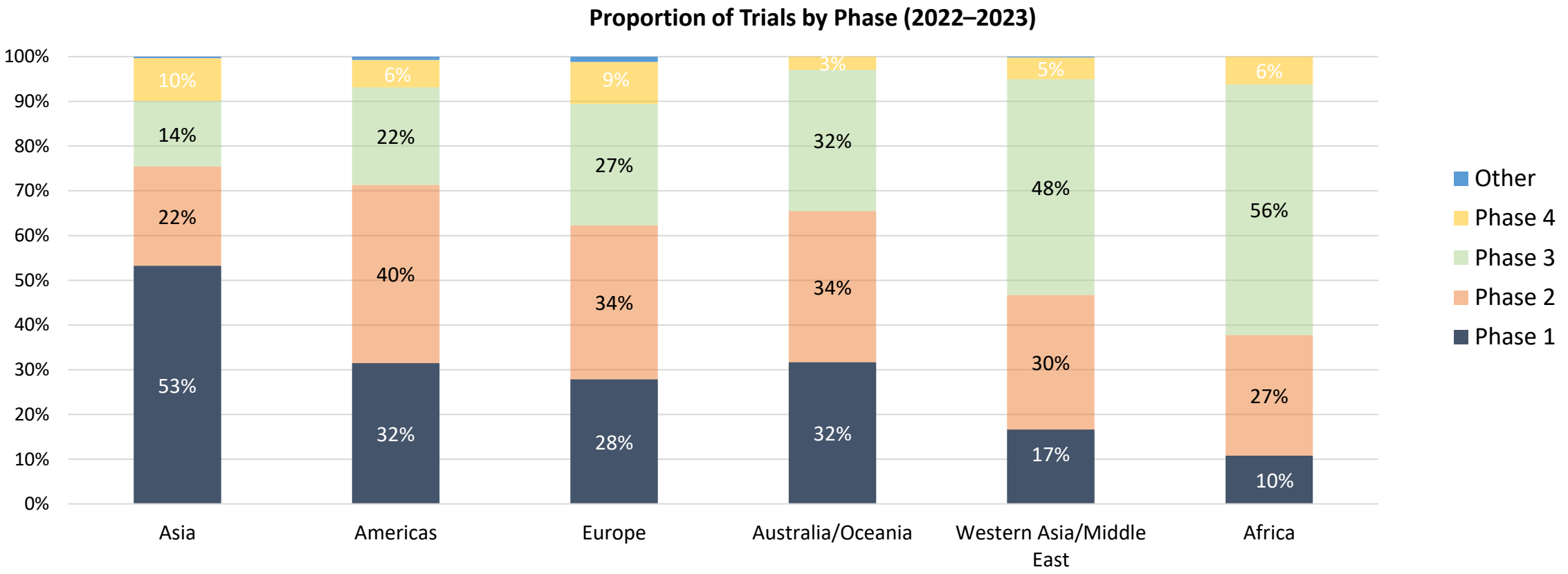
Percentage of Clinical Trials with Top 20 Pharma Involvement (2022–2023)



Sources: Citeline Trialtrove, Scrip; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 continent and may contribute to the counts for multiple continents; Western Asia/ Middle East is here considered a distinct continent and not included in the count for Asia; Scrip 100 Ranking used to segment companies; Top 20 companies by FY 2021 revenue; see Appendix for full company breakdown

Distribution by Phase

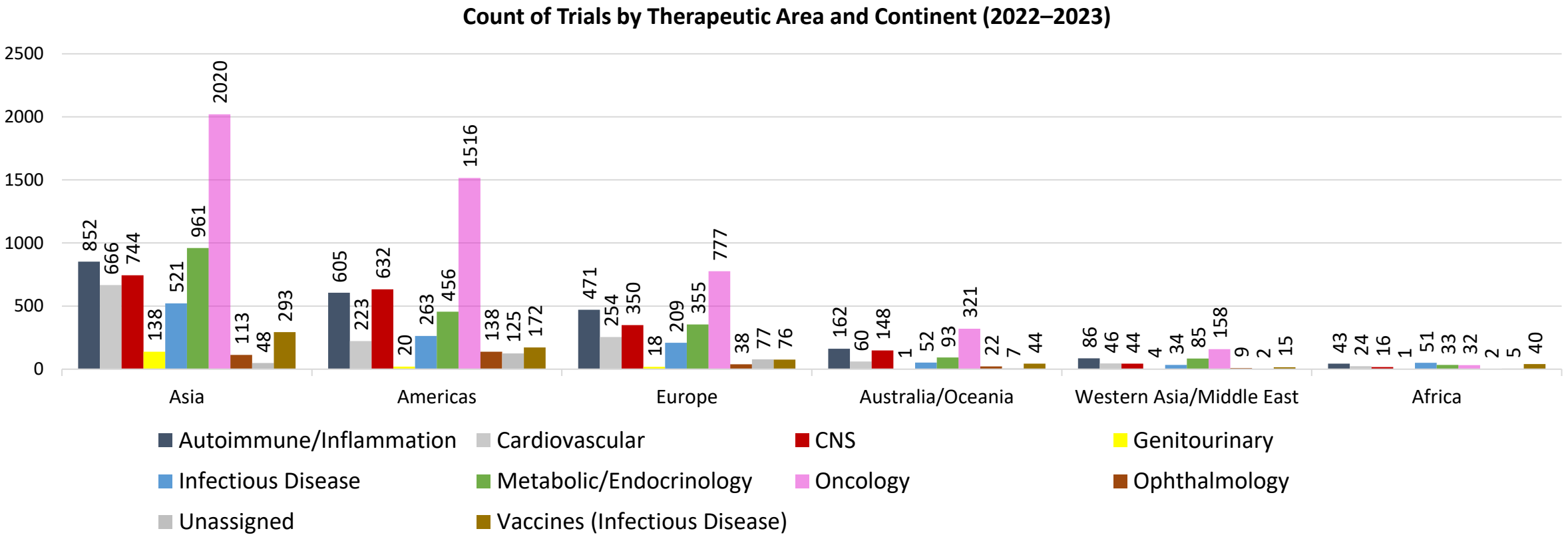
Trials in Europe and the Americas have a similar phase distribution, though studies in the Americas are less likely to be in Phase 3 vs European studies; Asia's trial phase coverage is highly polarized to Phase 1 trials



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 continent and may contribute to the counts for multiple continents; Western Asia/ Middle East is here considered a distinct continent and not included in the count for Asia; Other' refers to clinical trials that are not aligned with Phase 1, 2, 3 or 4 classifications; Data labels for "Other" not shown (as negligible)

Segmentation by Therapeutic Area

Oncology is the heaviest weighted therapeutic area in all continents other than Africa; studies in the genitourinary therapeutic area are least common across all continents



- A single trial may involve >1 therapeutic area and may contribute to the counts for multiple therapeutic areas
- A single trial may have sites in >1 continent and may contribute to the counts for multiple continents

Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; Western Asia/ Middle East is here considered a distinct continent and not included in the count for Asia; Unassigned' refers to trials that do not align with the listed Therapeutic Areas

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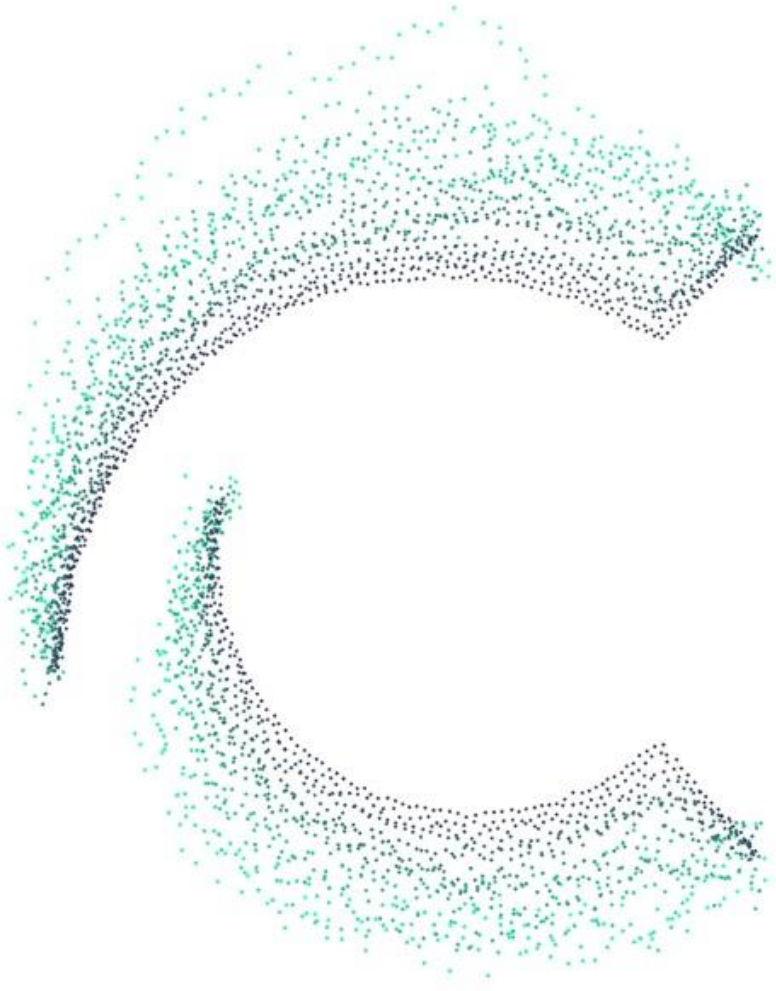
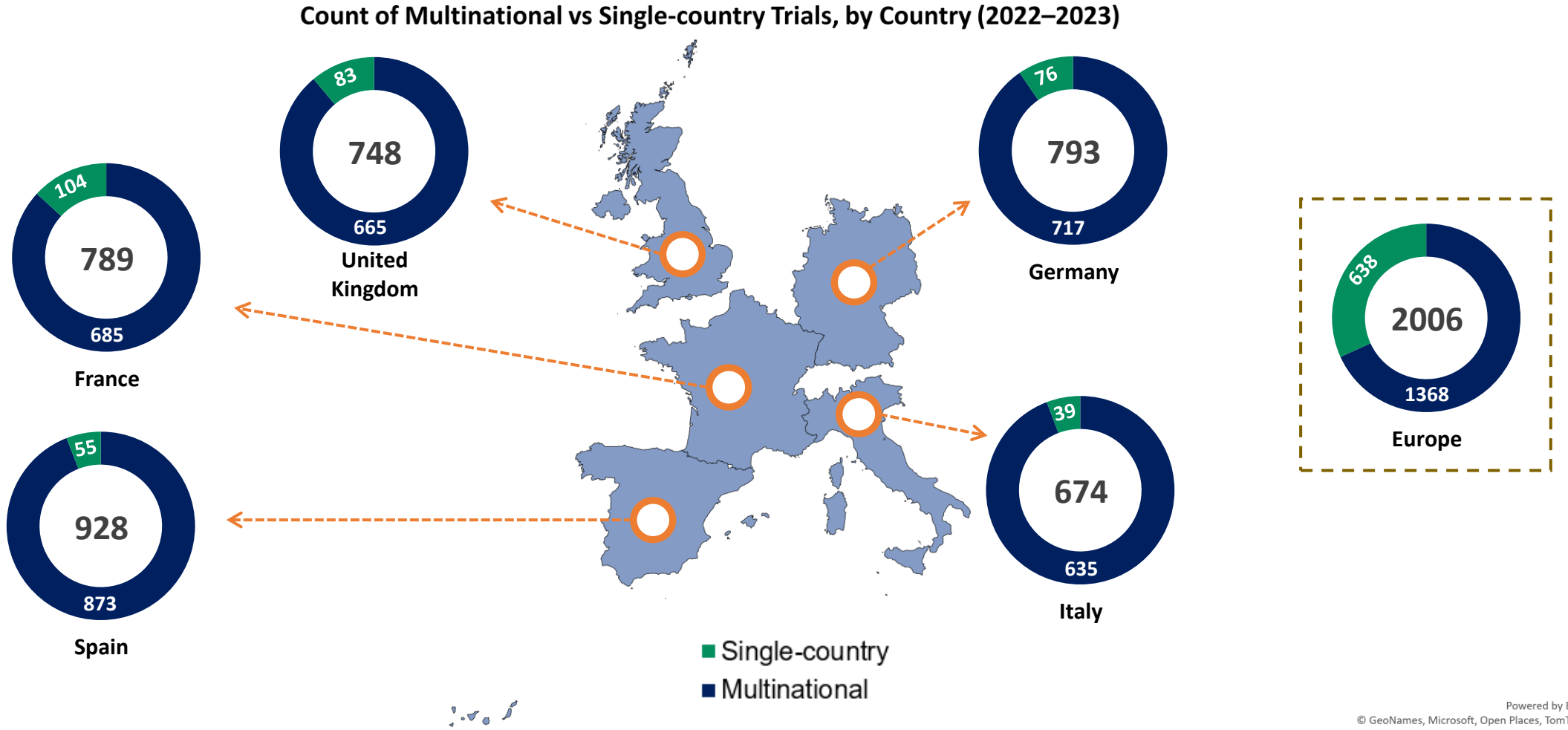
3. European Focus – Basic Picture



Multinational vs Single-Country Trials (2022 and S1-2023, industry and non-industry co-sponsors trials excluding HV trials)

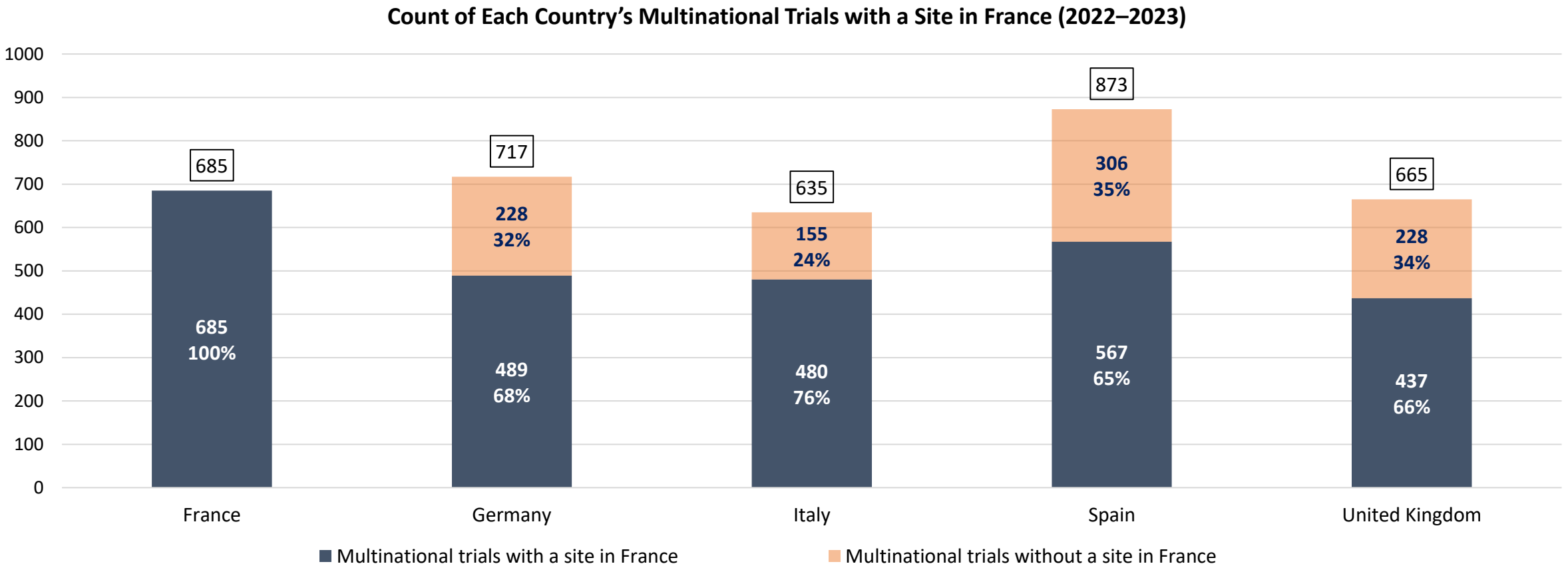
A greater proportion of trials with sites in France are multinational trials compared with the European average; nonetheless, France has a greater proportion of single-country trials than the EU4/UK comparators



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; Trials may have a non-industry co-sponsor; A single multinational study has sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once.

Multinational Trials with a Site in France

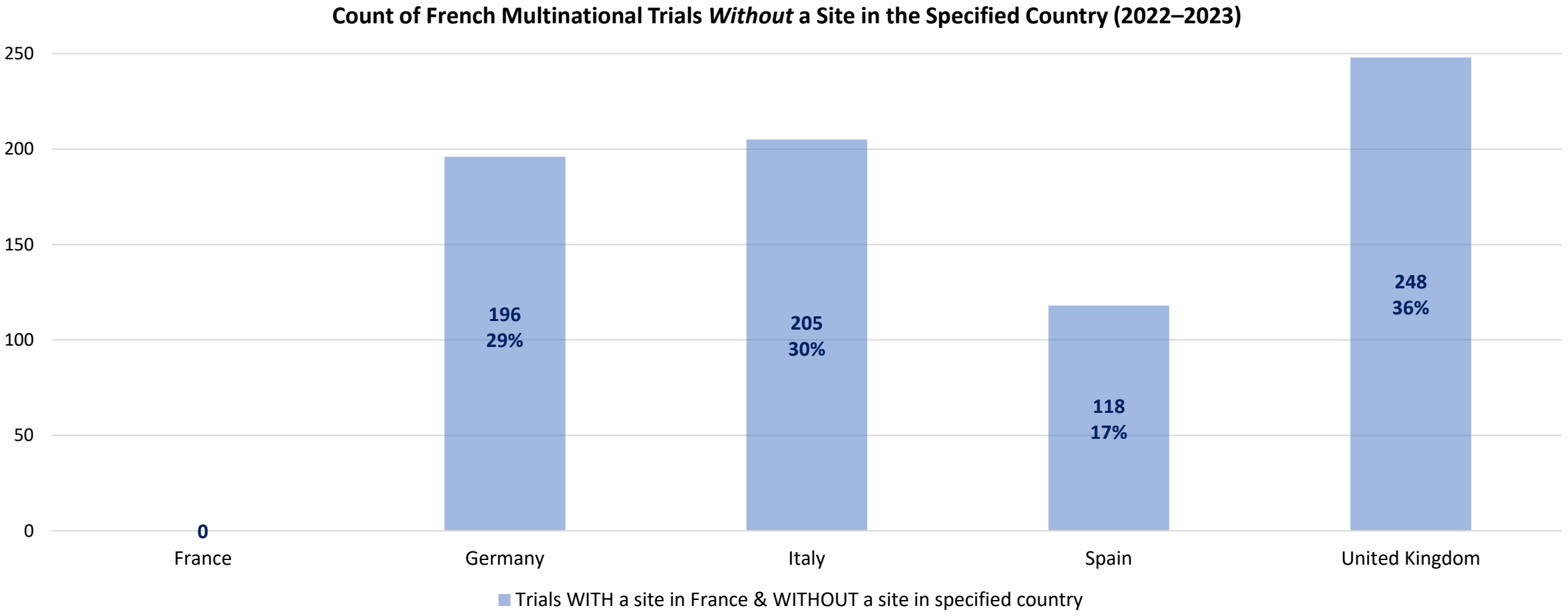
Trials with a site in Italy are most likely, of the comparator countries, to also have a site in France; trials with a site in Spain or the UK are least likely to also have site in France



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single multinational study has sites in >1 country and may contribute to the counts for multiple countries.

French Multinational Trials with No Sites in EU4 + UK

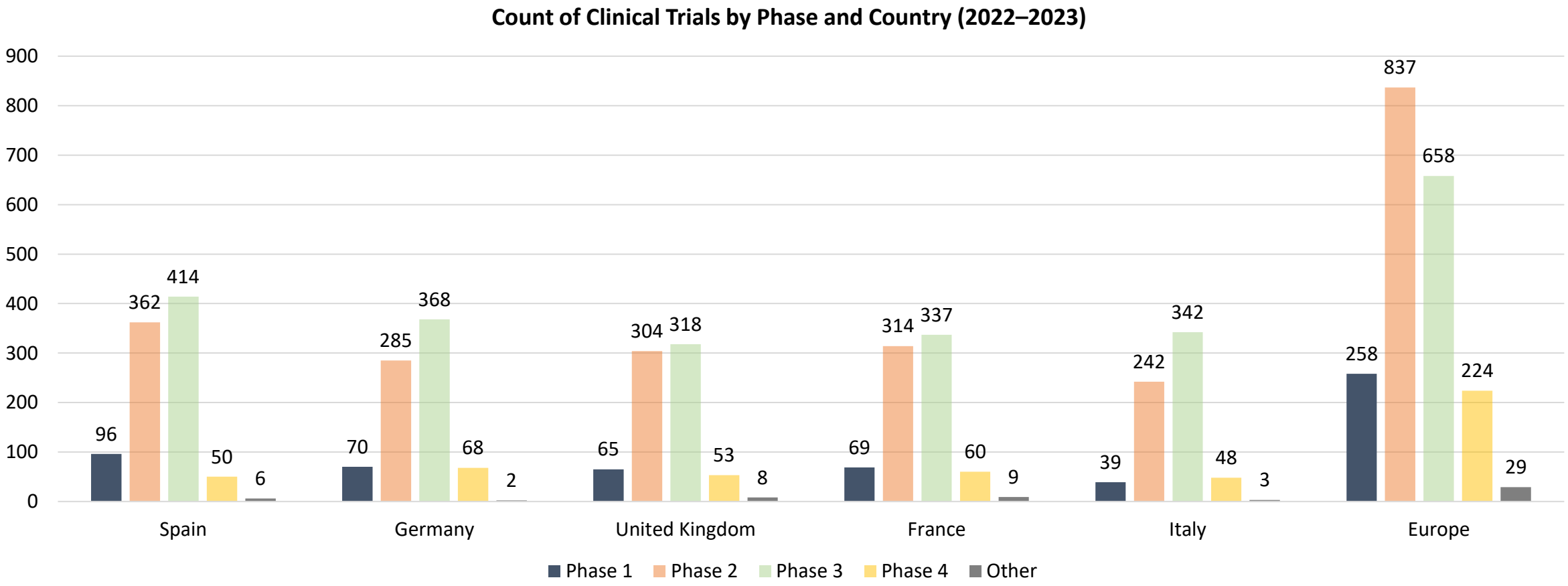
The 692 multinational trials with ≥1 site in France are least likely to have a site in the UK and most likely to have a site in Spain



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single multinational study has sites in >1 country and may contribute to the counts for multiple countries; By definition of the analysis, France has a count of zero

Trial Distribution by Phase

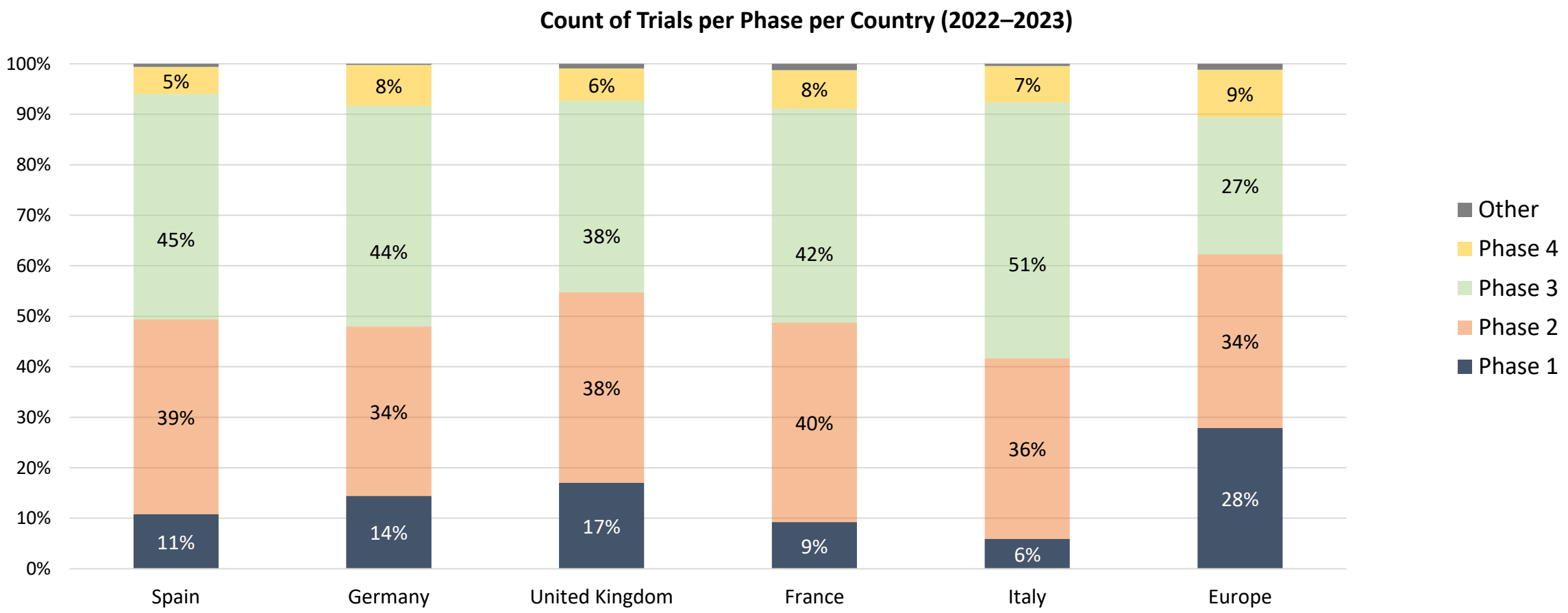
Spain's superiority in trial numbers exists across all phases except Phase 4; the relative distributions across phases are similar for all the comparator countries



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; 'Other' refers to Clinical Trials that do not align with Phase 1, Phase 2, Phase 3, or Phase 4 classification

Trial Distribution by Phase

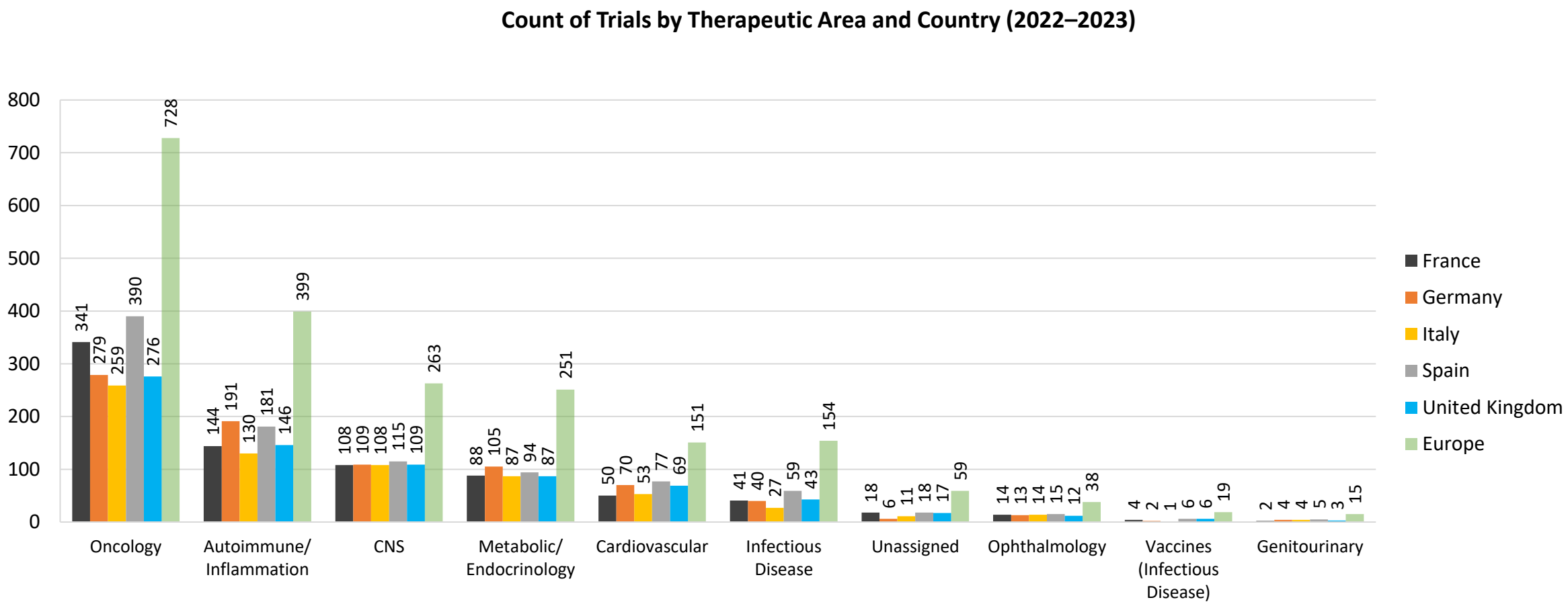
The EU4 + UK have a trial phase distribution that is more heavily weighted to Phase 3 compared with the European average



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; 'Other' refers to trials that do not align with Phase 1–4 classification; Data label for 'Other' not shown as negligible.

Trials by Therapeutic Area

France has the highest percentage of clinical trials in the oncology therapeutic area but the lowest percentage of trials in the autoimmune/inflammatory and cardiovascular therapeutic areas vs the EU4/UK comparators



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial may involve >1 therapeutic area and may contribute to the counts for multiple therapeutic areas; 'Unassigned' refers to trials that do not align with the listed therapeutic areas

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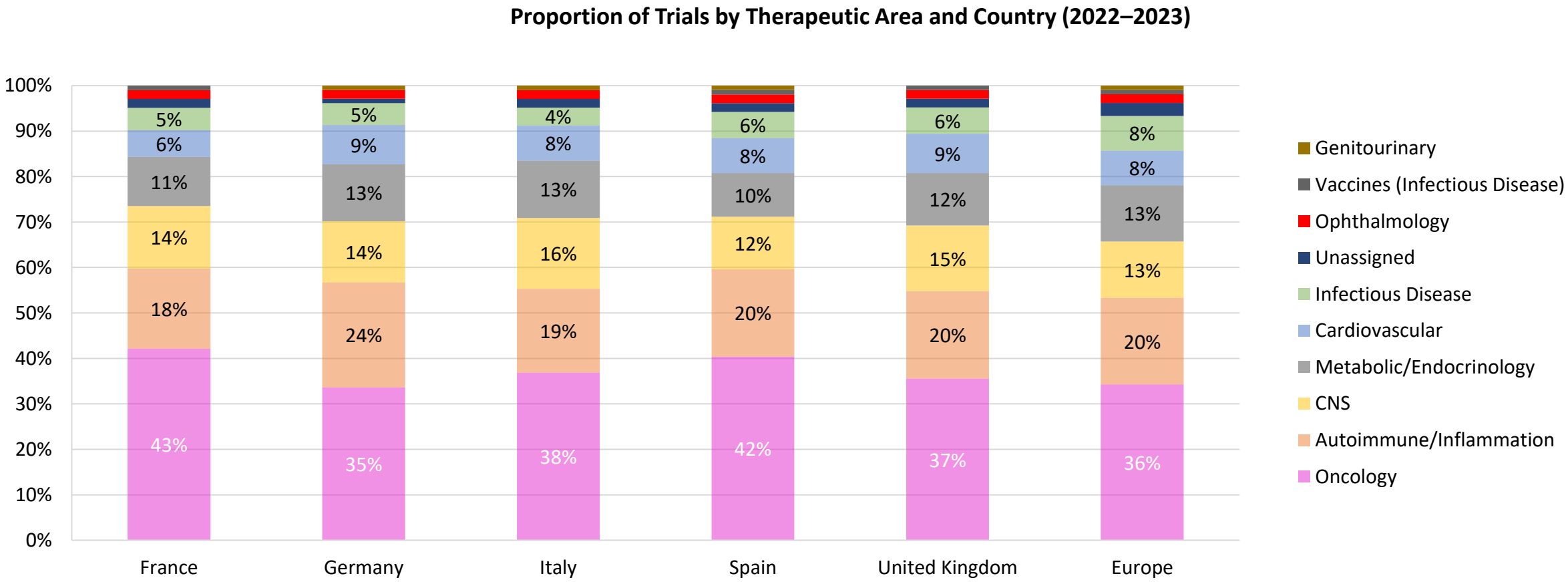
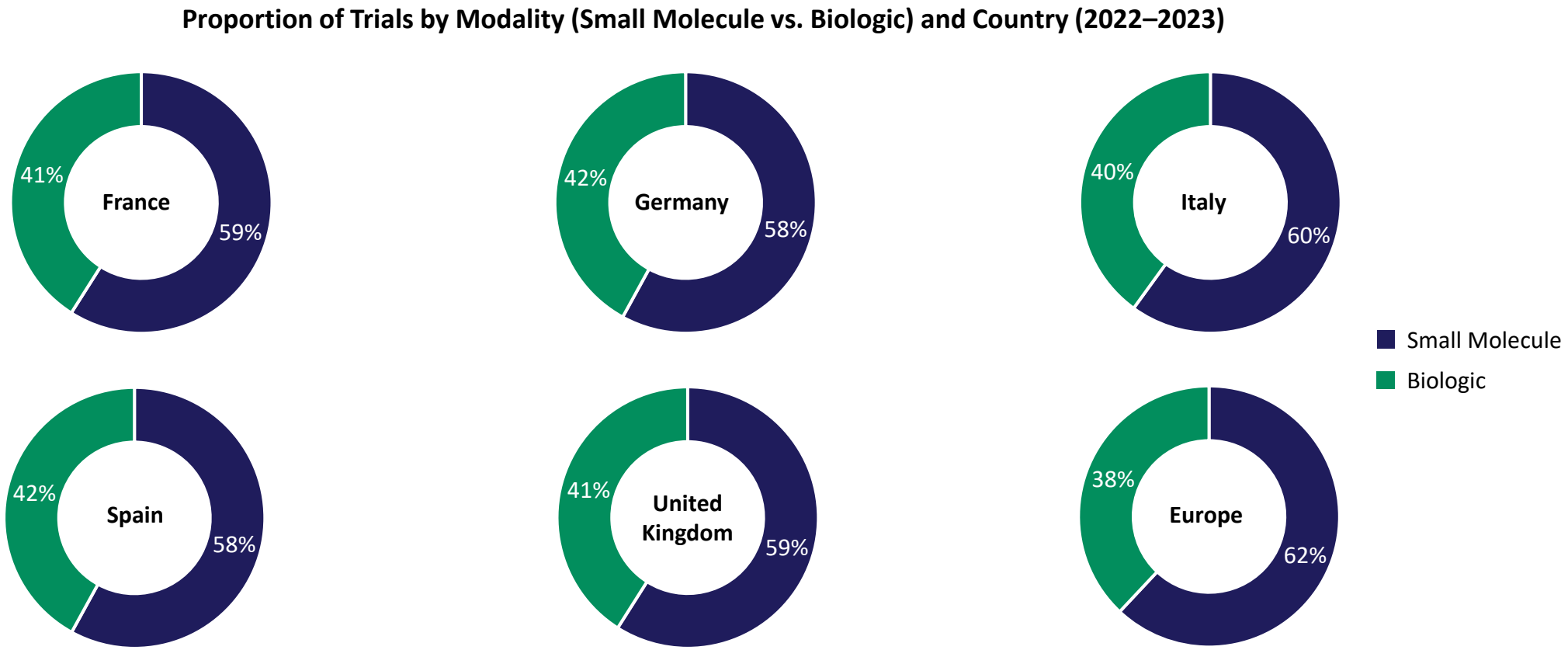


Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial may involve >1 therapeutic area and may contribute to the counts for multiple therapeutic areas; 'Unassigned' refers to trials that do not align with the listed therapeutic areas

Small Molecule vs Biologic (including healthy volunteer trials)

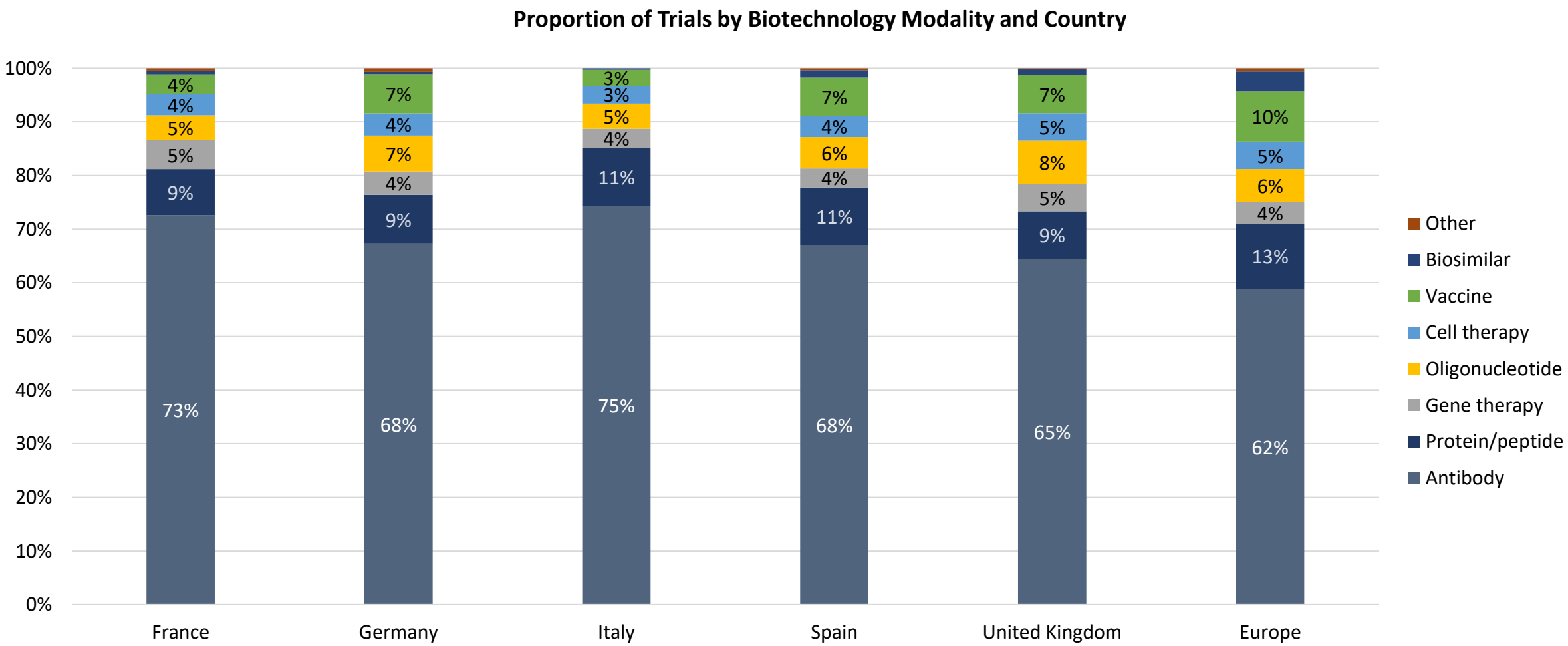
Across geographies, there is a similar ratio of small molecules to biologics being studied in trials



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country (but within the Europe category each trial is counted only once) and the corresponding drug(s) being investigated may contribute to the counts for multiple countries; A single trial may be investigating >1 drug

Trials by Biotechnology Modality (including healthy volunteer trials)

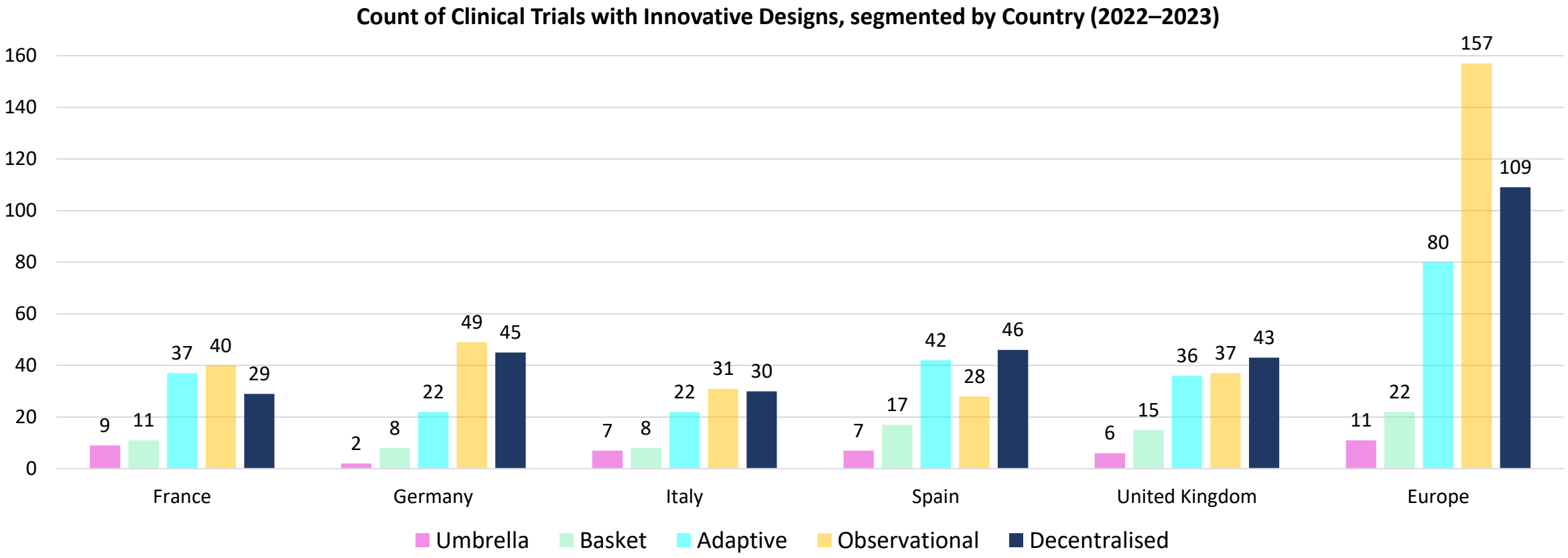
The proportions of biotechnology modalities being studied in trials are similar across the EU4 + UK, with antibodies comprising the most common modality in all geographies, followed by protein/peptides



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country (but within the Europe category each trial is counted only once) and the corresponding drug(s) being investigated may contribute to the counts for multiple countries; A single trial may be investigating >1 drug; A single drug can contribute to more than one of the listed modalities; Data label for “Other” category not shown as negligible.

Innovative Trial Designs (including healthy volunteer trials)

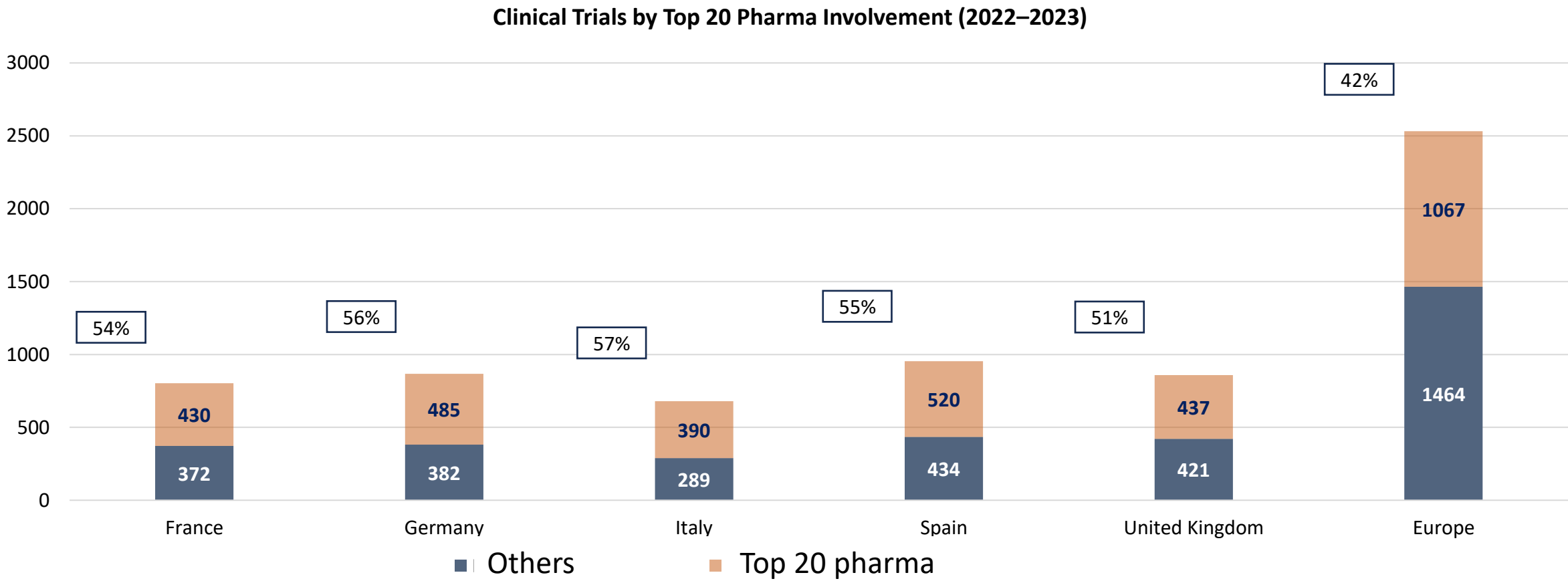
Umbrella studies are more prevalent in France than in comparator countries; France ranks 2nd in number of observational and adaptive studies but decentralized studies are relatively uncommon



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial can involve >1 innovative design type and therefore contribute to the counts for multiple categories.

Extent of Top 20 pharma Involvement (including healthy volunteer trials)

Clinical trials have a comparable percentage of Top 20 Pharma involvement across the EU4 + UK; all 5 of these countries have a greater level of trial involvement from Top 20 Pharma compared with the European average



Sources: Citeline Trialtrove, Scrip; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Scrip 100 Ranking used to segment companies; "Big Pharma" = Top 20 companies by FY 2021 revenue, Mid Pharma = Top 21-40 companies by FY 2021 revenue, all other companies considered Biotech; see Appendix for full company breakdown

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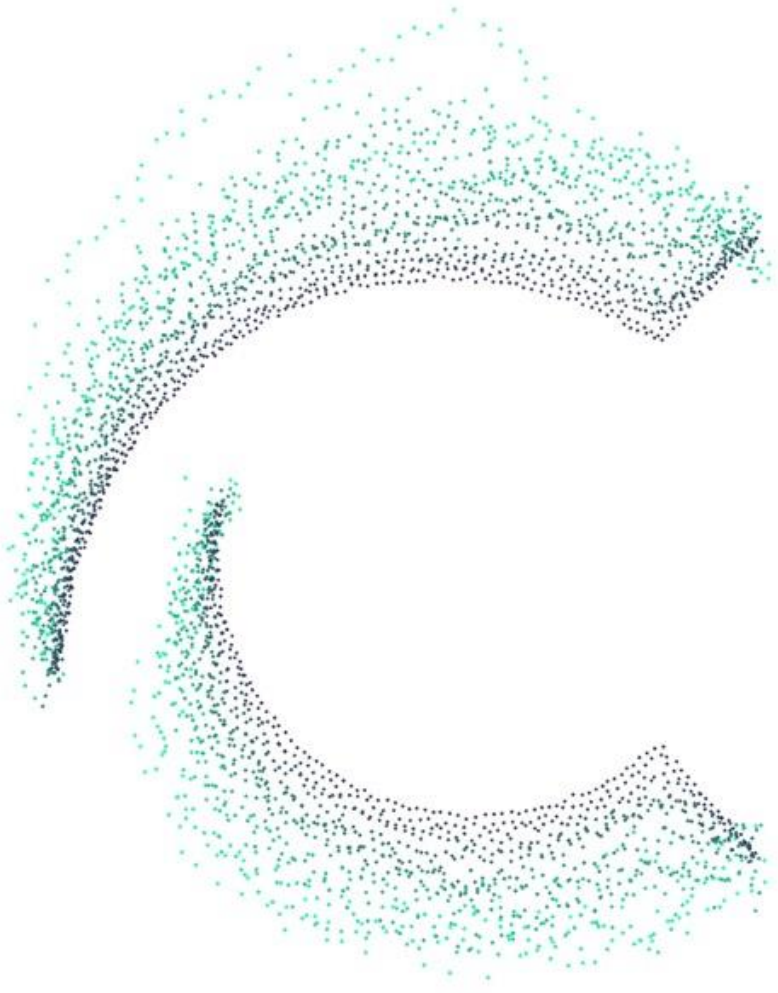
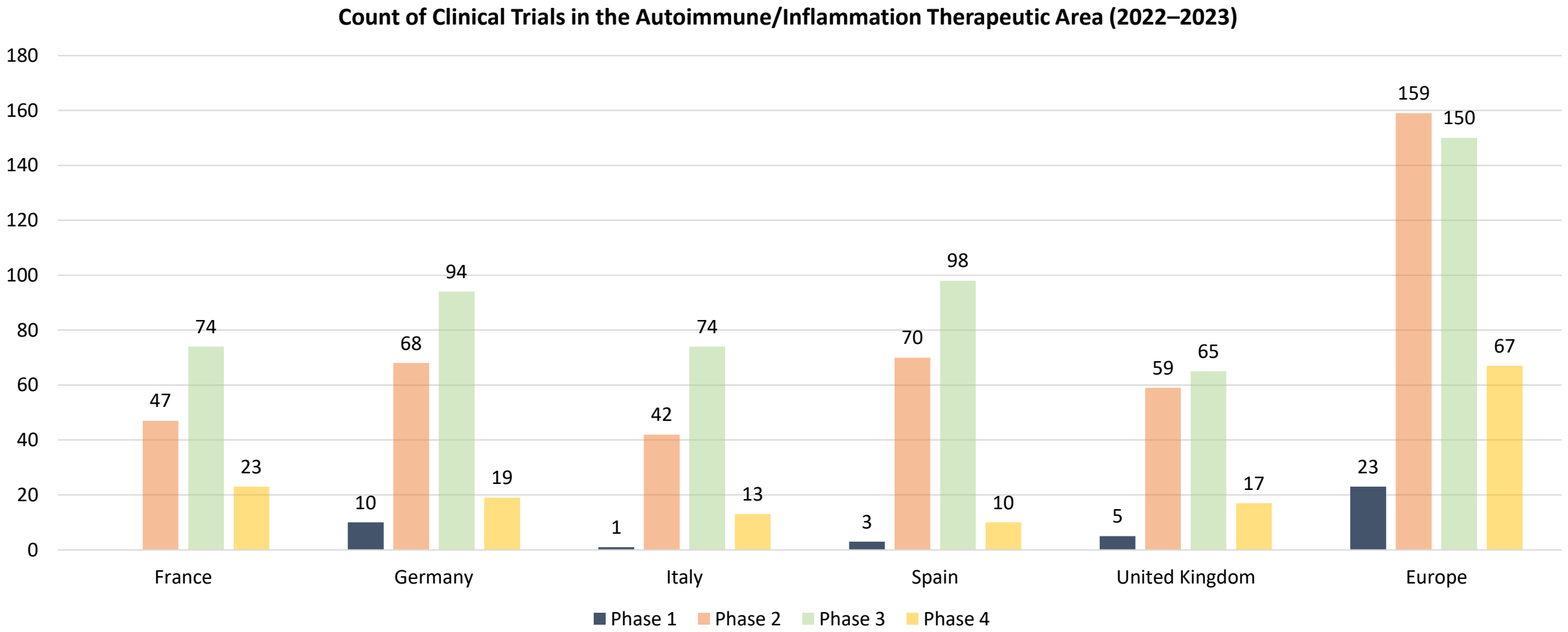
4. European Focus – Therapeutic Area Deep Dive



Autoimmune/Inflammation TA by Phase (excluding HV trials)

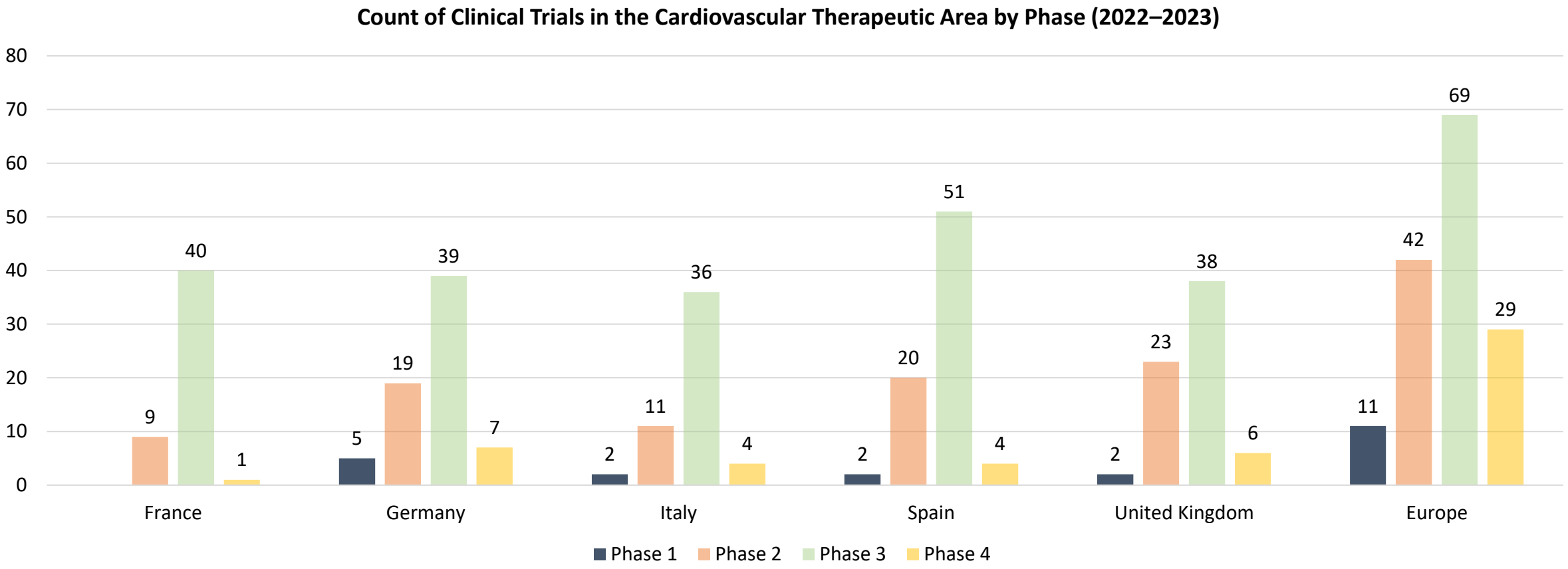
Phase 1 trials are most prominent in Germany; France leads the comparator set in Phase 4 trials



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

Cardiovascular TA by Phase (excluding healthy volunteer trials)

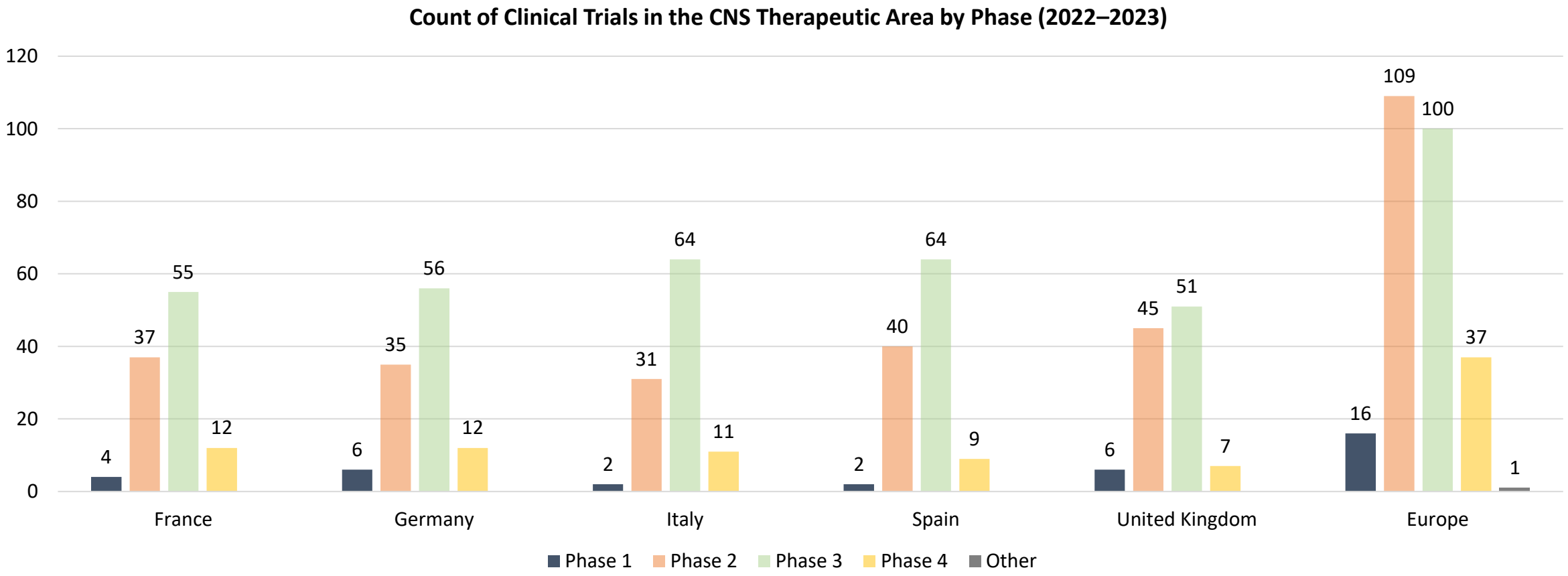
Germany has the largest number of Phase 1 trials; France ranks last among the comparator set for Phase 2 trials, narrowly behind Italy



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

CNS TA by Phase (excluding healthy volunteer trials)

The UK has the greatest number of Phase 2 Clinical Trials in the CNS therapeutic area; Spain and Italy dominate Phase 3 Clinical Trials



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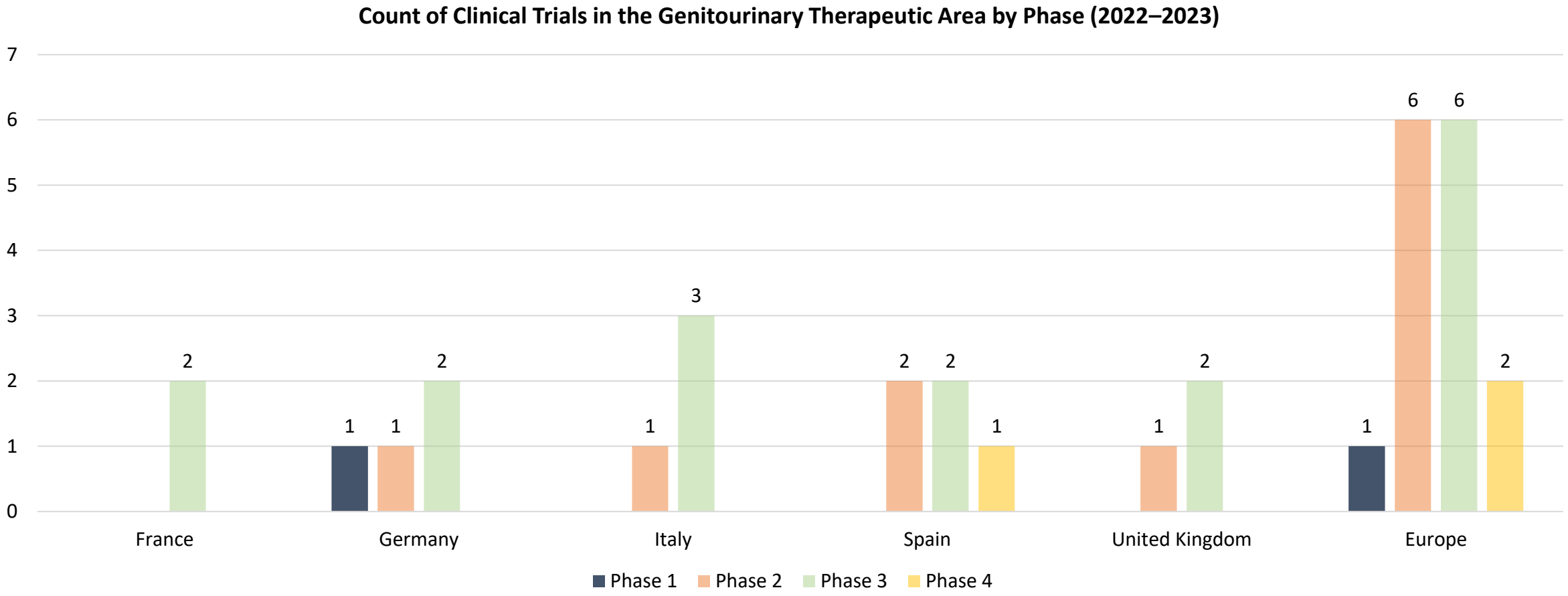
Genitourinary TA by Phase (excluding healthy volunteer trials)

None of the EU4 + UK countries has a prominent position in the sparsely investigated genitourinary therapeutic area



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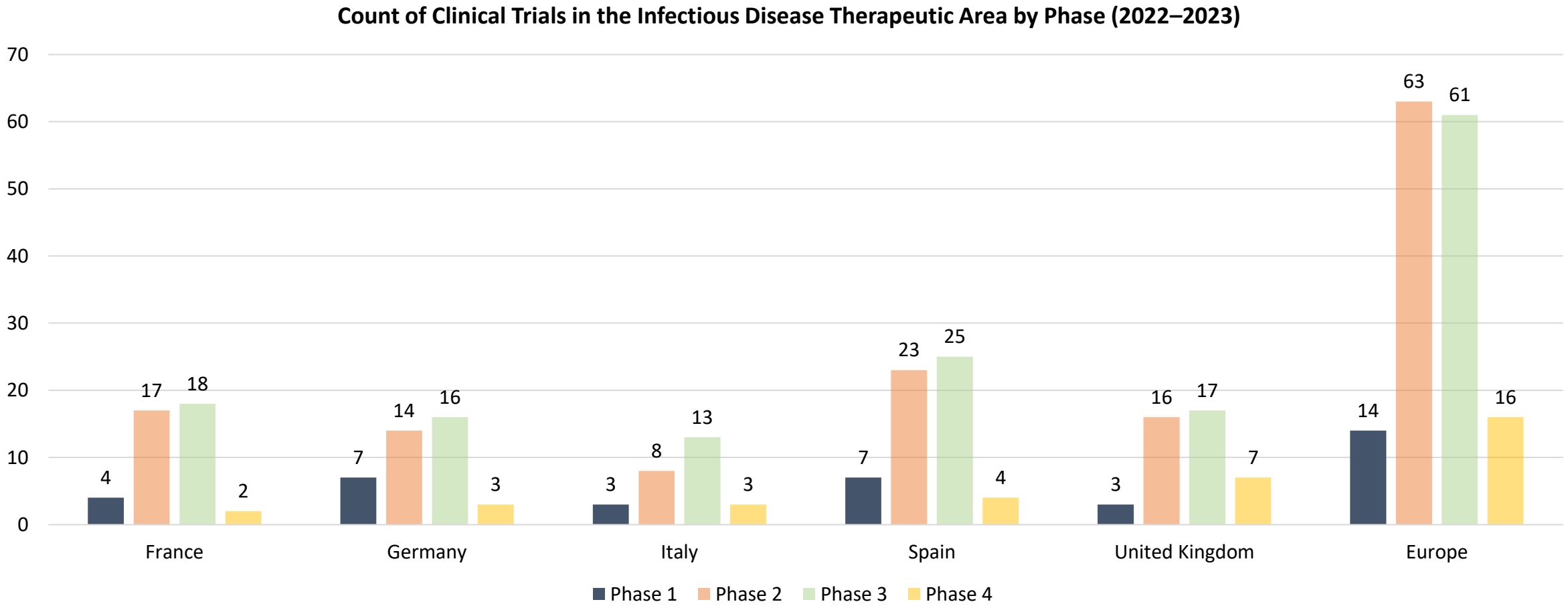
Infectious Disease TA by Phase (excluding healthy volunteer trials)

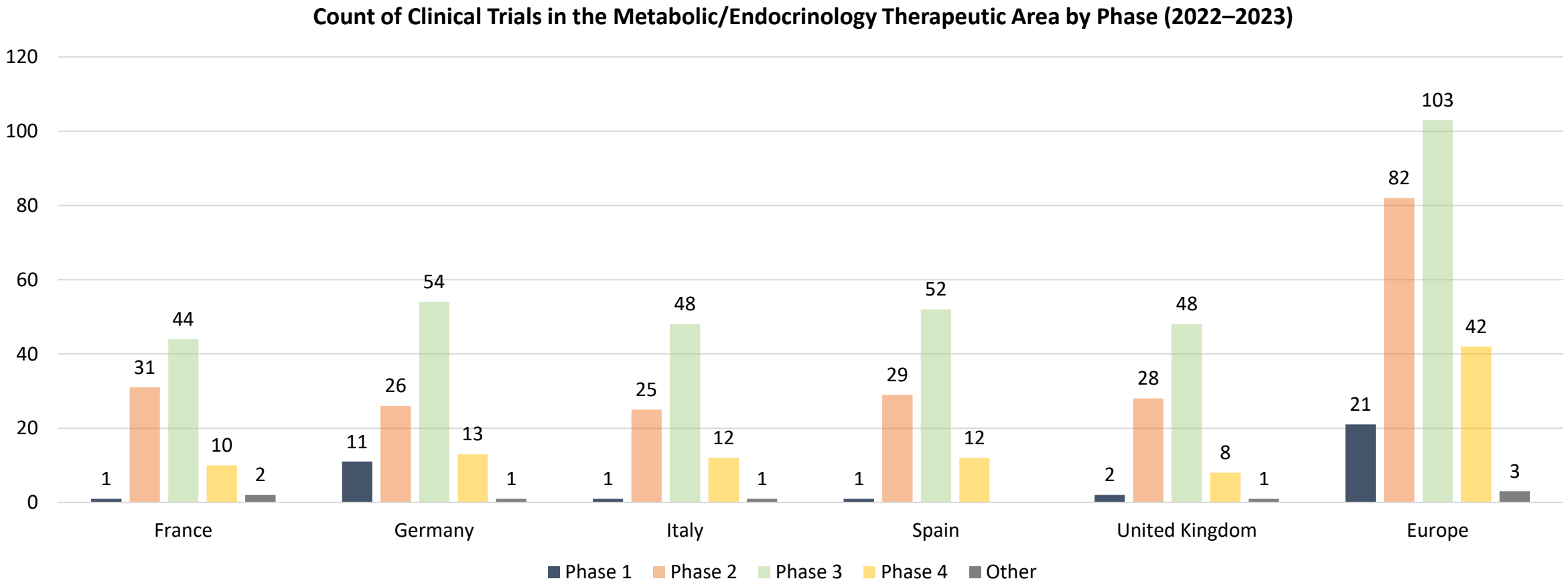
Spain leads Phase 3 in infectious diseases; France ranks second among the comparator countries for infectious disease trials at Phase 2 & Phase 3



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

Metabolic/Endocrinology TA by Phase (excluding healthy volunteer trials)

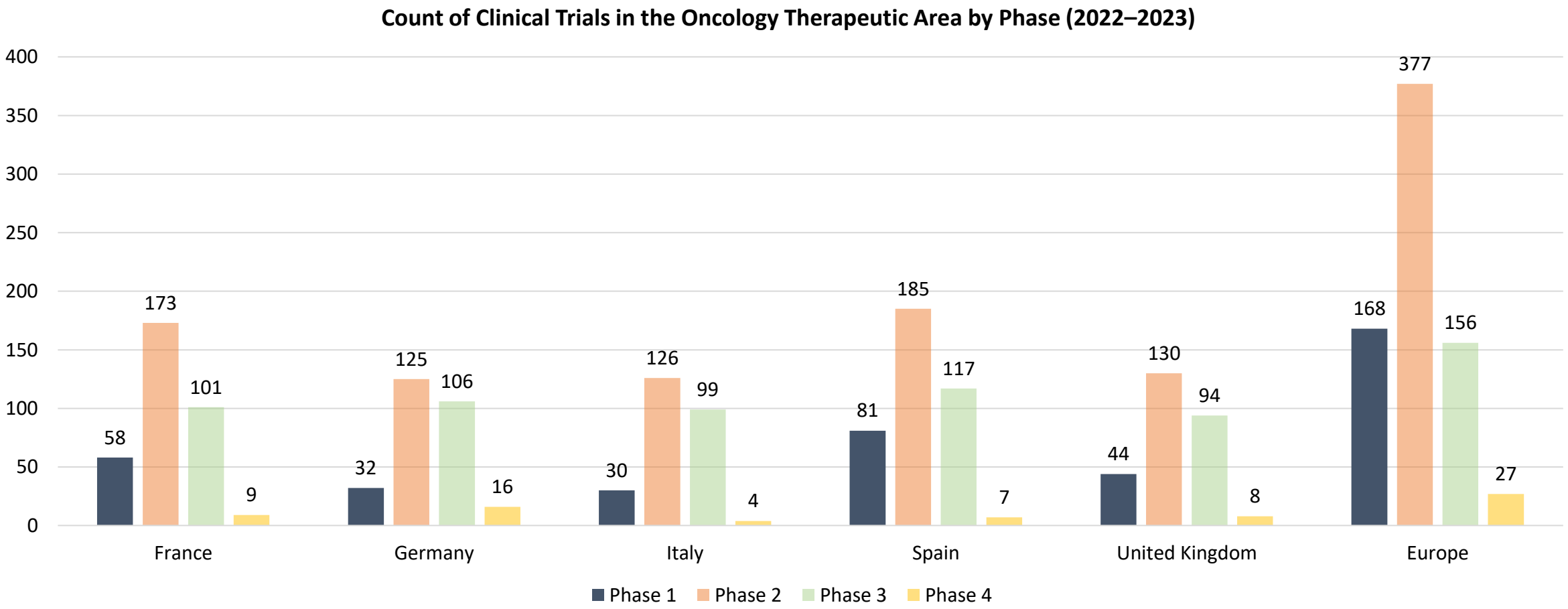
The comparator countries have similar numbers of trials at Phase 2, 3, and 4; only Germany has significant numbers at Phase 1



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

Oncology TA by Phase (excluding healthy volunteer trials)

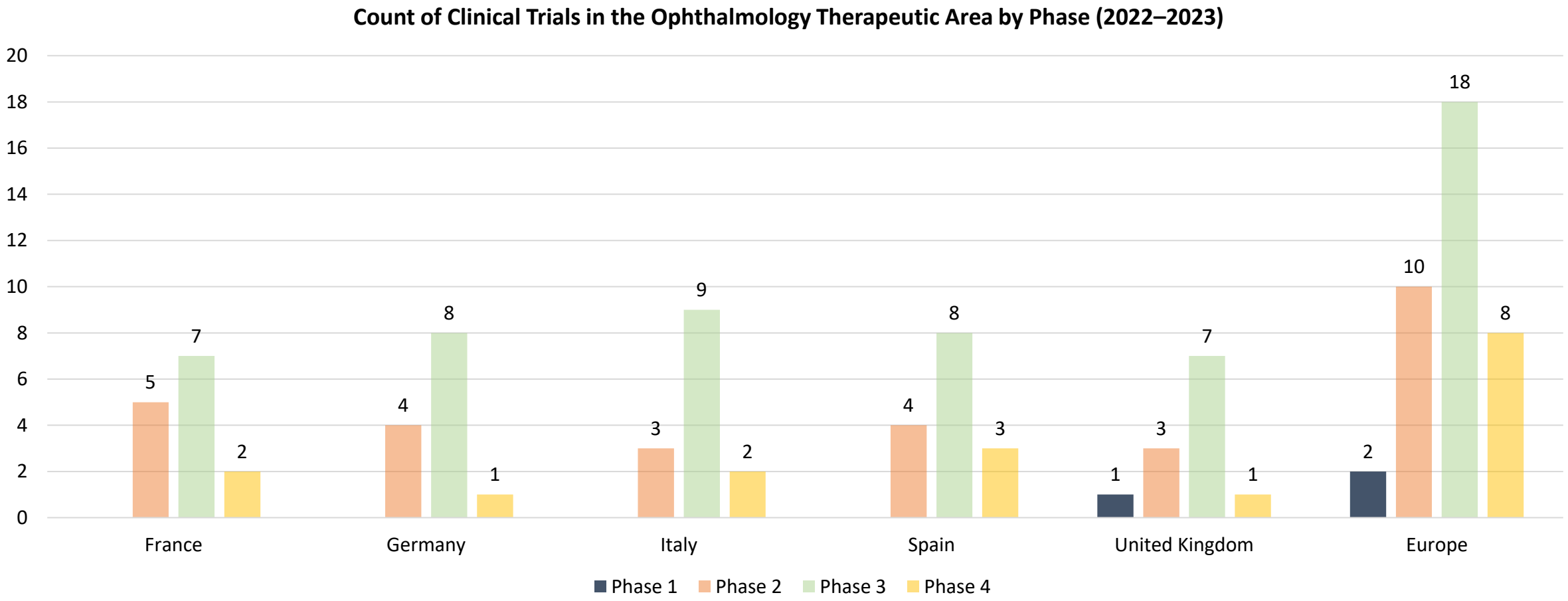
France ranks 2nd behind Spain for the number of early-stage clinical trials in the oncology therapeutic area; Spain also leads in Phase 3 studies, followed by Germany, and France



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

Ophthalmology TA by Phase (excluding HV trials)

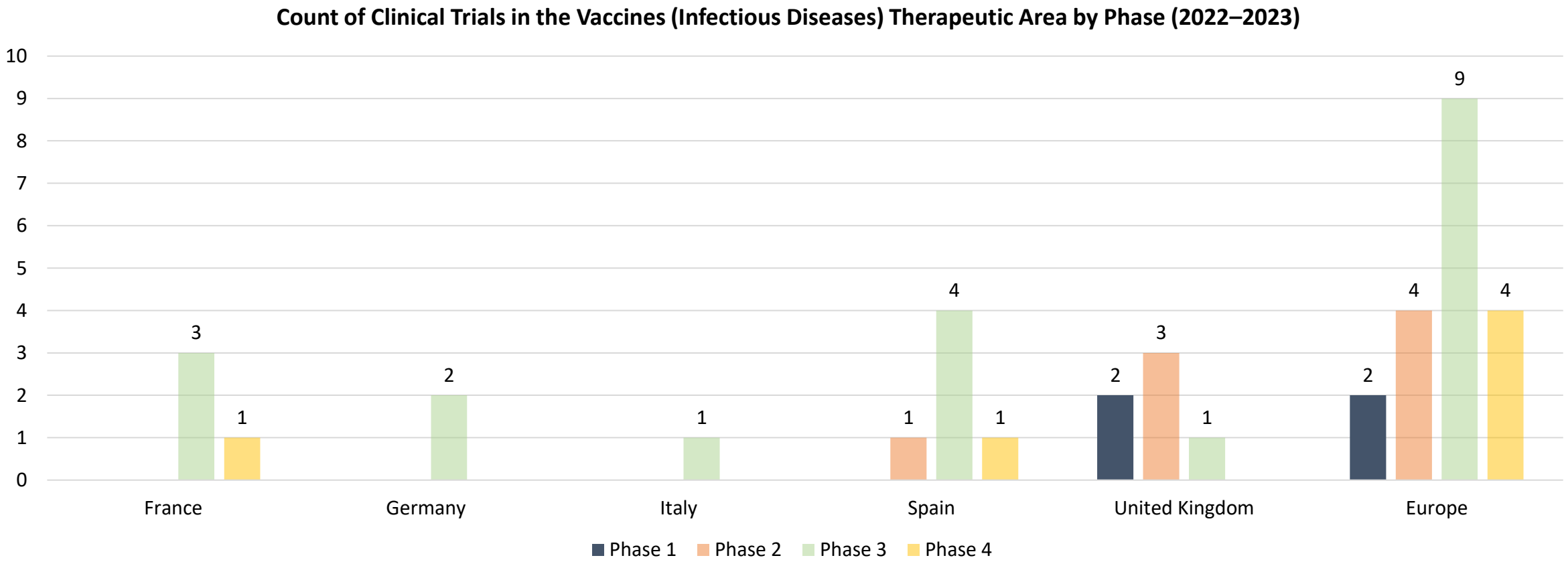
There are few clinical trials in the ophthalmology therapeutic area across Europe; a similar phase distribution exists across all the comparator countries in this TA



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

Vaccines (Infectious Diseases) TA by Phase (excluding HV trials)

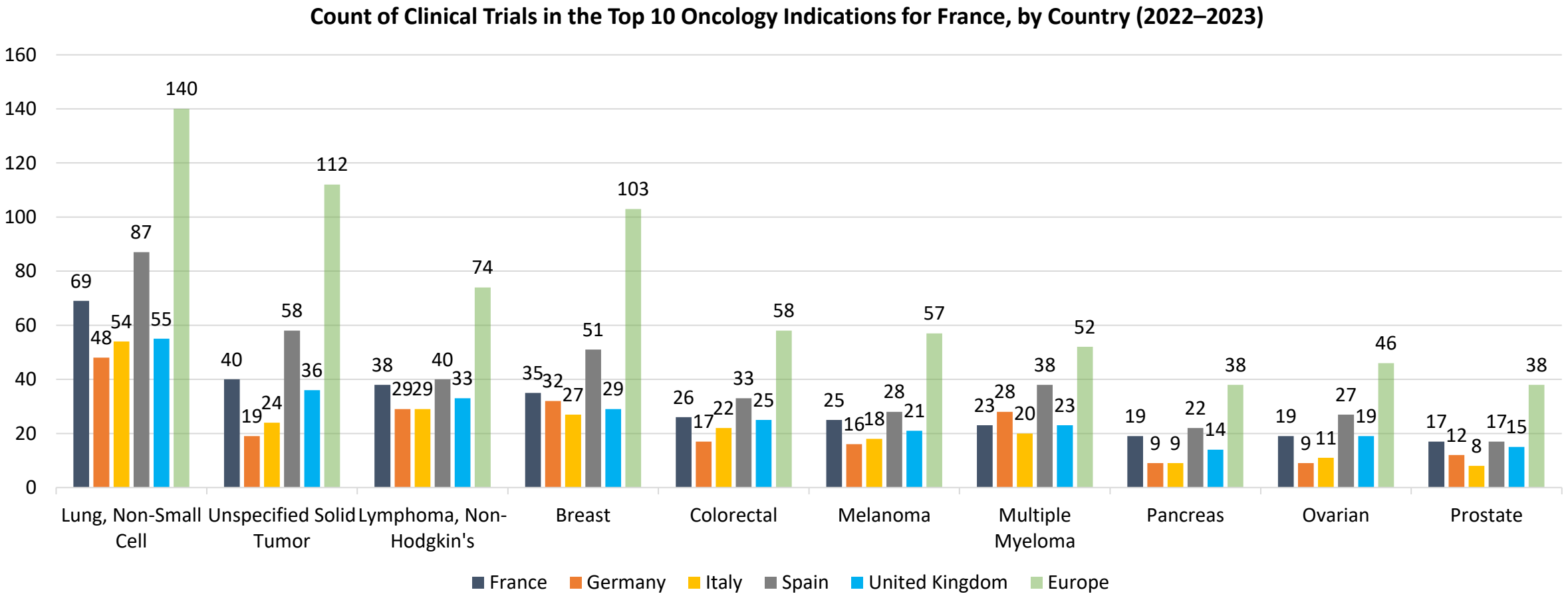
This therapy area has very low numbers of trials when healthy volunteer trials are excluded



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; Healthy Volunteer studies have been excluded

Therapy Area Analysis – Oncology Focus

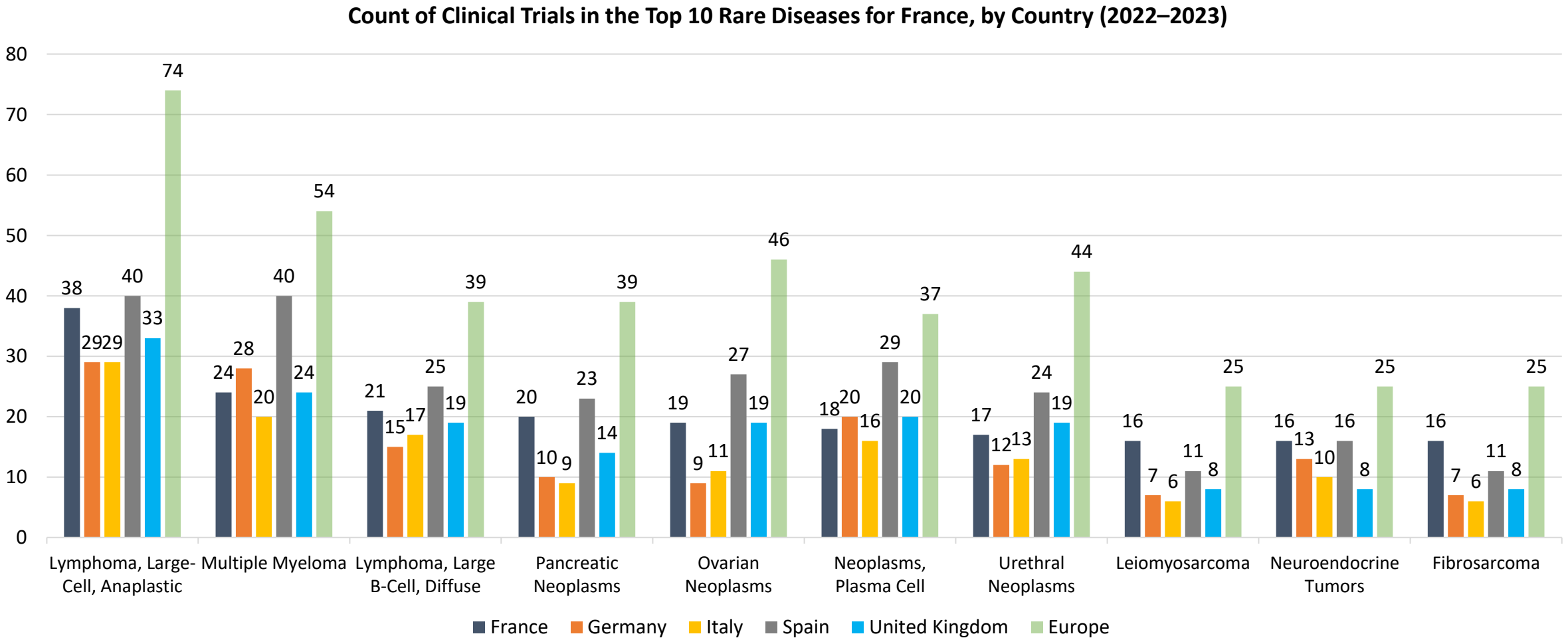
NSCLC is the most common oncology indication for trials in France, by a substantial margin; NHL and multiple myeloma are the only two hematalogic malignancies in the top 10



Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; ; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial may involve >1 oncology indication and may contribute to the counts for multiple oncology indications

Therapy Area Analysis – Rare Disease Focus

The 10 rare diseases most commonly studied in trials with sites in France are dominated by oncology indications; in most of these diseases, Spain has the most trials



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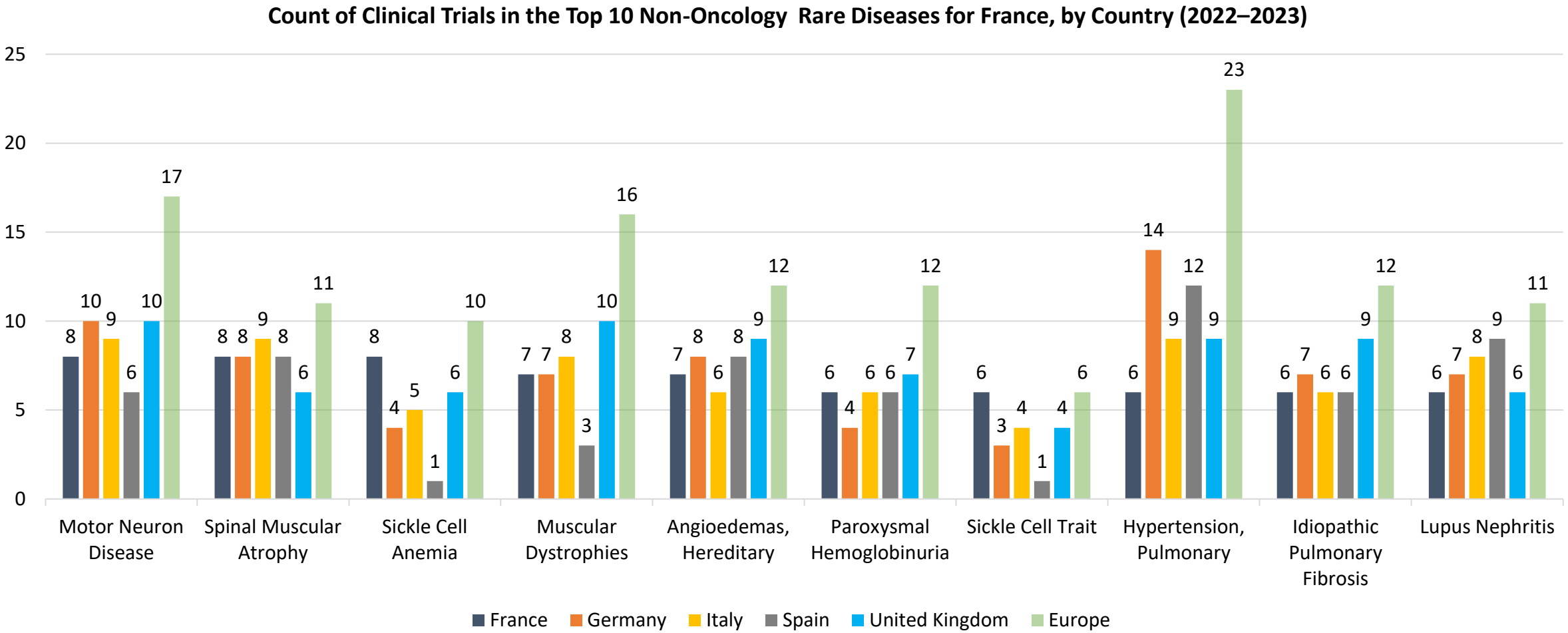
Therapy Area Analysis – Non-Oncology Rare Diseases

When excluding oncology indications, the joint most studied rare diseases in France are motor neuron disease (ALS), spinal muscular atrophy, and sickle cell anemia



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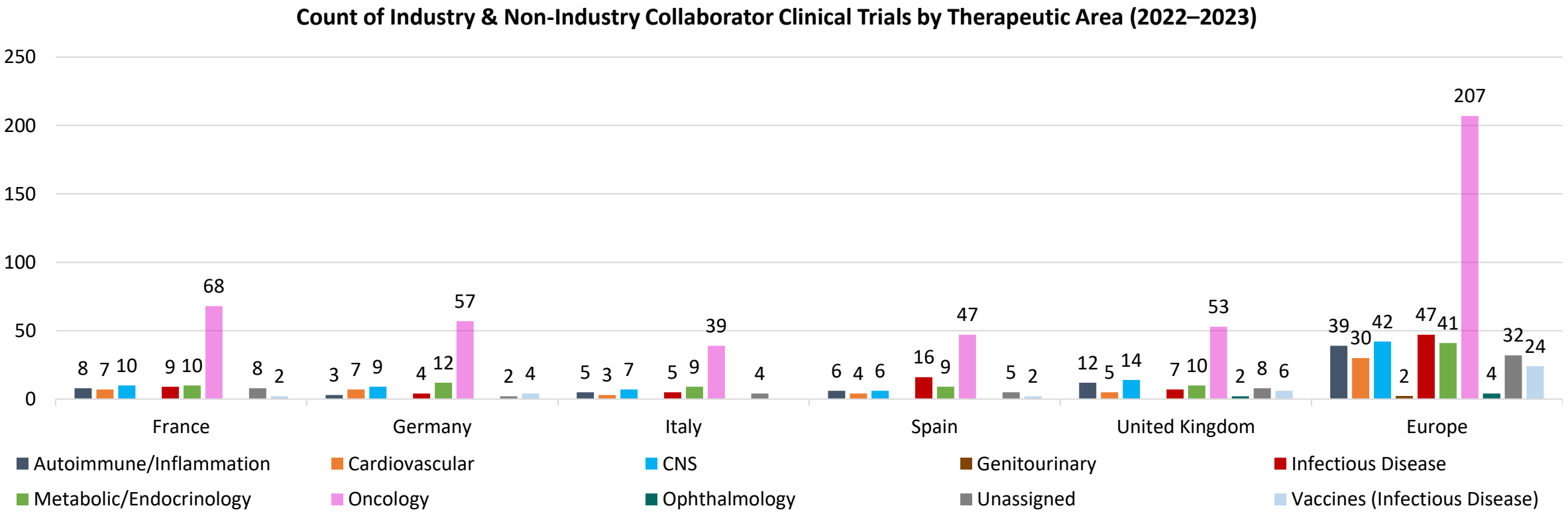
Trials with Industry Sponsor + Non-Industry Collaborator (including HV trials)

Trials with industrial sponsors and any non-industry collaborator type are most common in oncology and infectious diseases; France leads in oncology studies, Spain in infectious disease studies

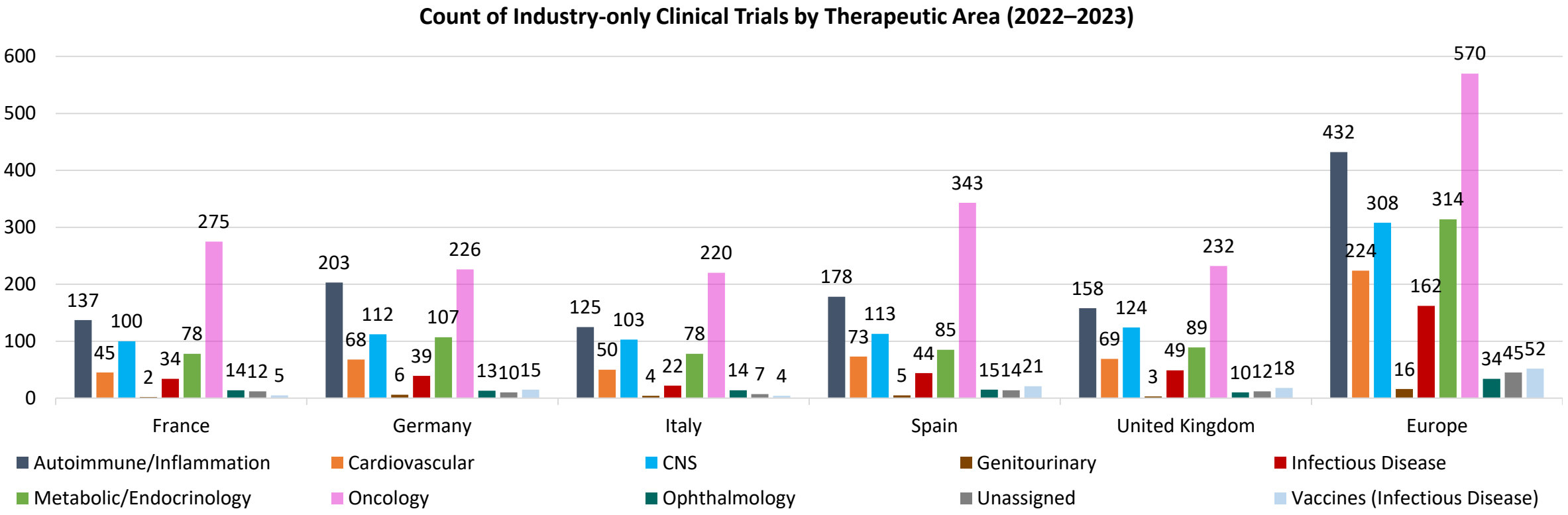


- Trials have at least one industry sponsor and at least one collaboration with academic / not for profit funding entity / cooperative group / unassigned / government / miscellaneous / natural products, OTC, cosmetics sponsor type

Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial may involve >1 therapeutic area and may contribute to the counts for multiple therapeutic areas

Trials with Industry Sponsor Only (including healthy volunteer trials)

Trials with only industrial sponsors are centered on oncology and autoimmune/inflammation; Spain leads in the number of oncology studies, Germany leads in the number of autoimmune/inflammation studies

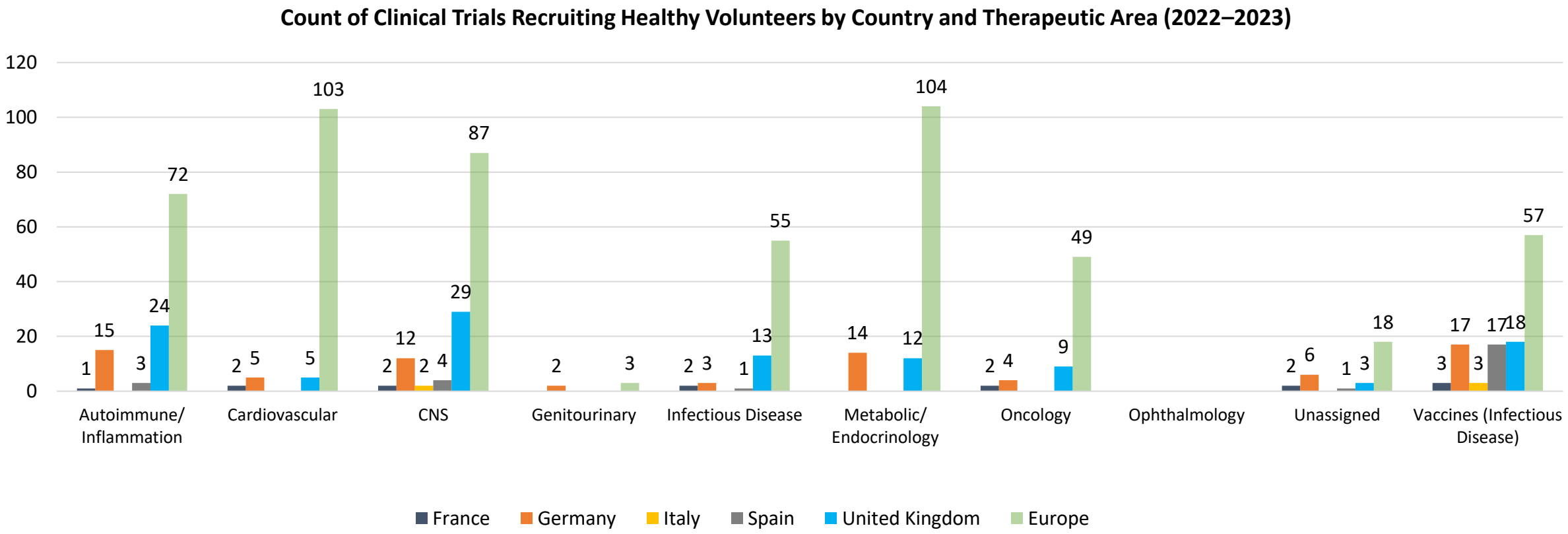


- Trials have at least one industry sponsor and no collaboration with academic / not for profit funding entity / cooperative group / unassigned / government / miscellaneous / natural products, OTC, cosmetics sponsor type

Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial may involve >1 therapeutic area and may contribute to the counts for multiple therapeutic areas

Healthy Volunteer Studies

Trials with a healthy volunteer arm are most common in the UK; CNS studies recruit healthy volunteers most frequently across the comparator countries, although CV and metabolic trials dominate Europe-wide



- Includes only trials with at least one arm of healthy volunteers

Sources: Citeline Trialtrove; Notes: Data set comprises all industrially sponsored trials with a start date from 1/1/2022 to 30/6/2023; A single trial may have sites in >1 country and may contribute to the counts for multiple countries, but within the Europe category each trial is counted only once; A single trial may involve >1 therapeutic area and may contribute to the counts for multiple therapeutic areas

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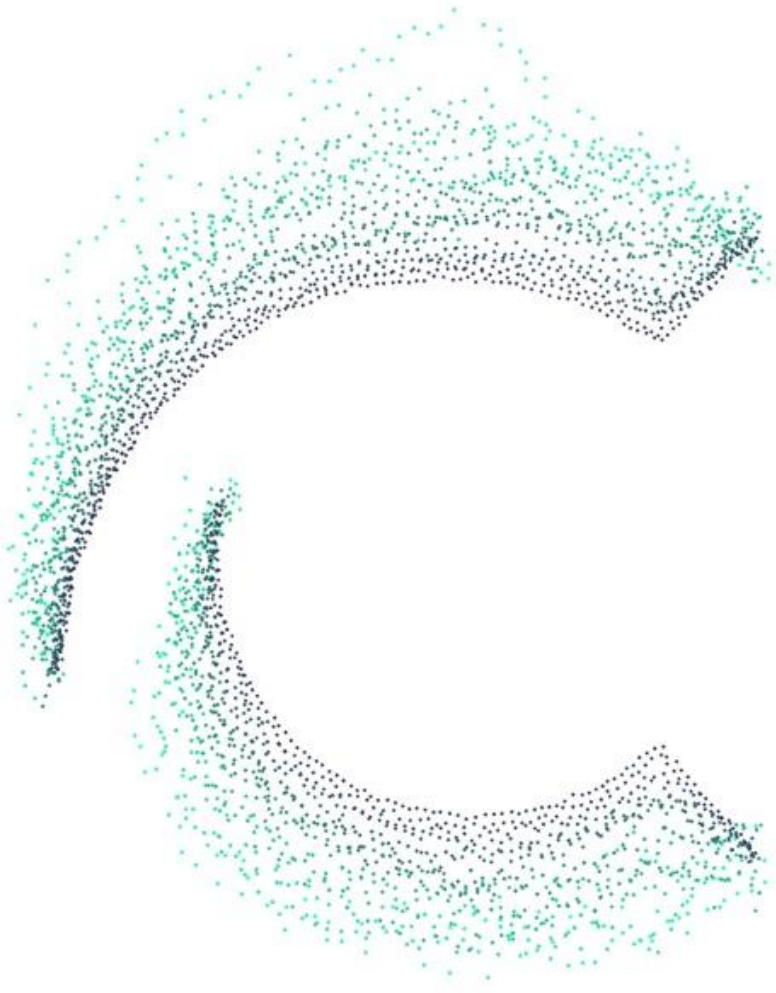
5. Appendix



Company Type – Company Breakdown

Big Pharma, Mid Pharma, and Biotech classification sourced from Scrip, Citeline's global news and insights team

Big Pharma	Mid Pharma
Pfizer	Moderna
AbbVie	Regeneron
Johnson & Johnson	Teva
Novartis	Baxter International
Roche	Astellas Pharma
Bristol-Myers Squibb	Biogen
Merck & Co.	CSL Limited
Sanofi	Otsuka Holdings
AstraZeneca	Fresenius
GlaxoSmithKline	Bausch Health
Takeda	Merck KGaA
Eli Lilly	Vertex Pharmaceuticals
Gilead Sciences	Eisai
Amgen	UCB
BioNTech	Servier
Novo Nordisk	Sun Pharmaceutical Industries
Bayer	Grifols
Sinovac Biotech	Abbott
Boehringer Ingelheim	Sumitomo Dainippon Pharma
Viatris	Shanghai Fosun Pharmaceutical

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CITELINE COMMERCIAL

Outlook 2023

The Scrip 100 universe gathers 2021 financial performance data and compares the activities of the top biopharma businesses, ranked by pharmaceutical sales.

Sources: Citeline Pharmaprojects, Scrip

Attractivité de la France pour la recherche clinique

Focus sur l'activité française

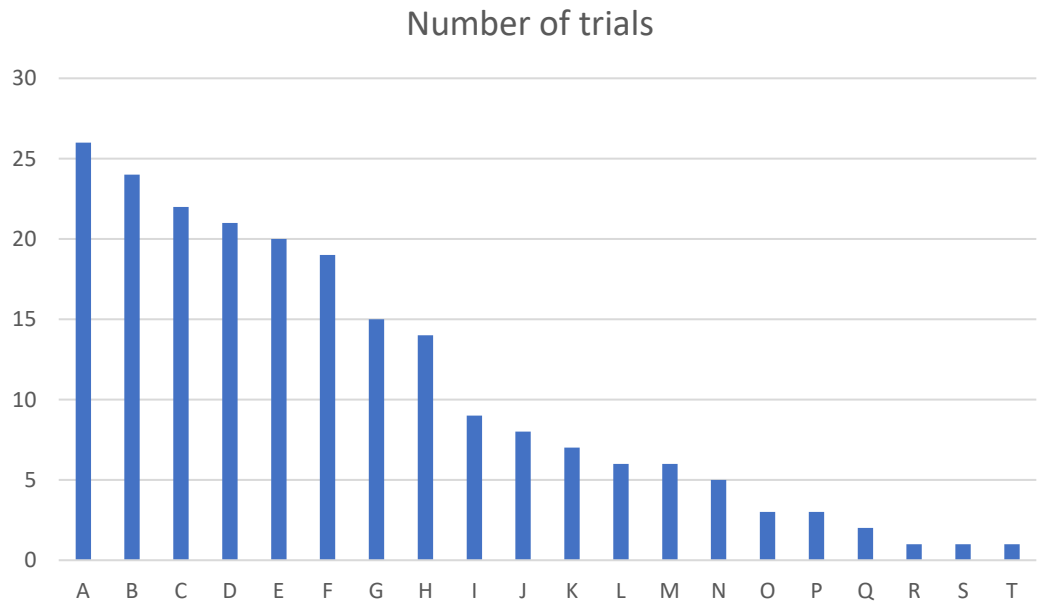
Analyse de la base OSCAR

Caractérisation de l'échantillon issu de la base du Leem « OSCAR »

Volet délais

214 essais cliniques analysés

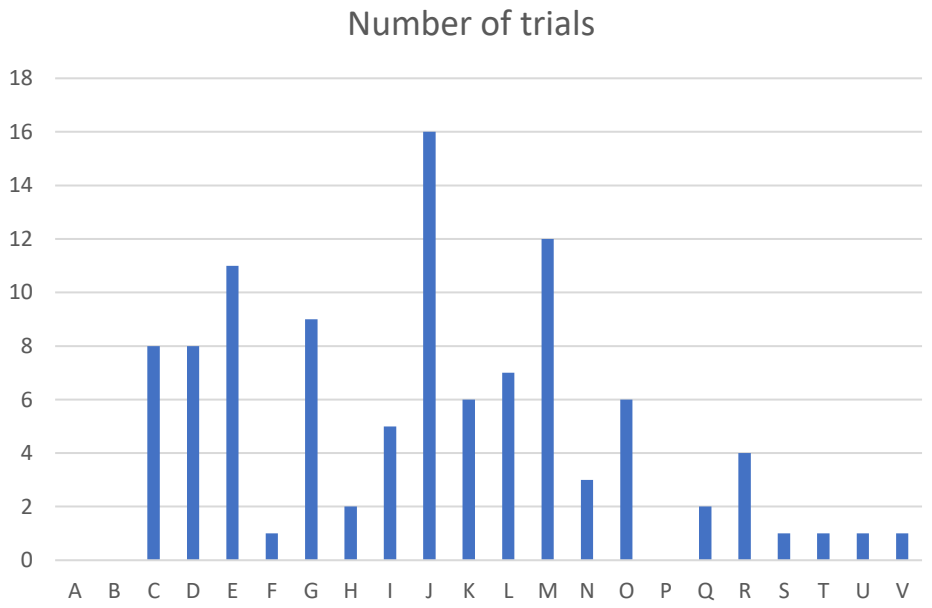
Renseignés par 20 entreprises ou CROs



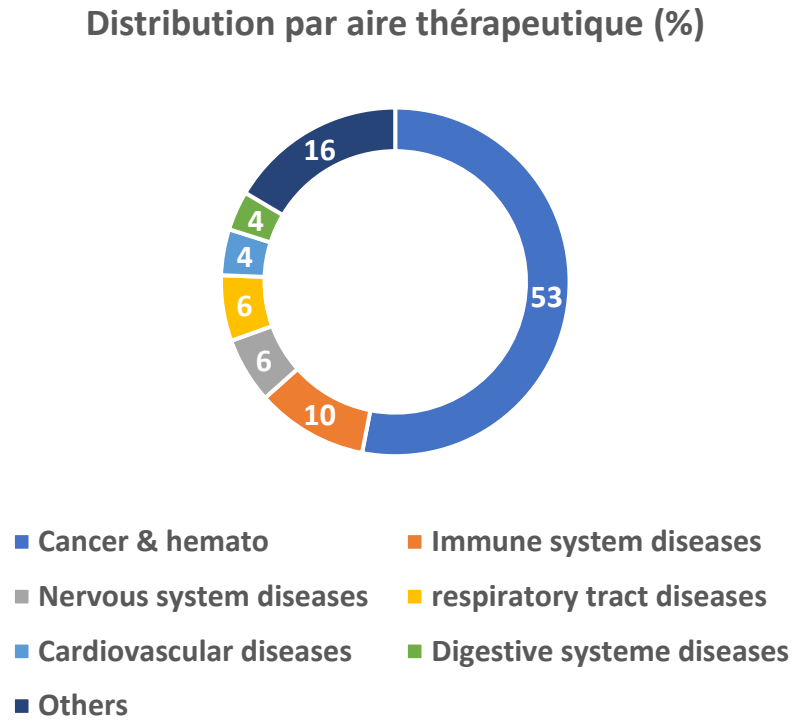
Volet inclusions

106 essais cliniques analysés

Renseignés par 19 entreprises ou CROs



Caractérisation de l'échantillon issu de la base du Leem « OSCAR »
Volet « autorisation »: 214 essais renseignés par 20 promoteurs ou CROs



- 10 % Maladies rares
- 4 % Médicaments de Thérapie Innovante
- 12 % avec enfants
- 46% avec seniors

Entrée en vigueur du règlement EU N°536/2014 (CTR) avec utilisation optionnelle du portail européen (CTIS) entre le 31/01/2022 et le 31/01/2023 puis obligatoire à compter du 01/02/2023.

Concomitance de deux voies d'autorisation (Loi Jardé et CTR) sur la période analysée.

Les entreprises ayant majoritairement continué d'utiliser la Loi Jardé, les délais présentés rendent compte d'une évaluation par l'ANSM et les CPP (sur 164 essais).

L'échantillon d'essais déposés dans le CTIS (50 essais) permet de présenter quelques premières tendances.

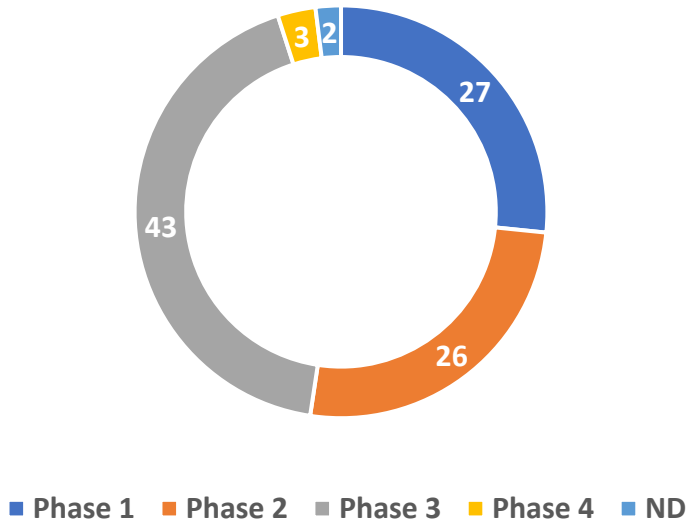
Caractérisation de l'échantillon issu de la base du Leem « OSCAR »
Volet « autorisation »: sous-échantillon dit « Loi Jardé »

Dépôt au sein du SI RIPH 2G

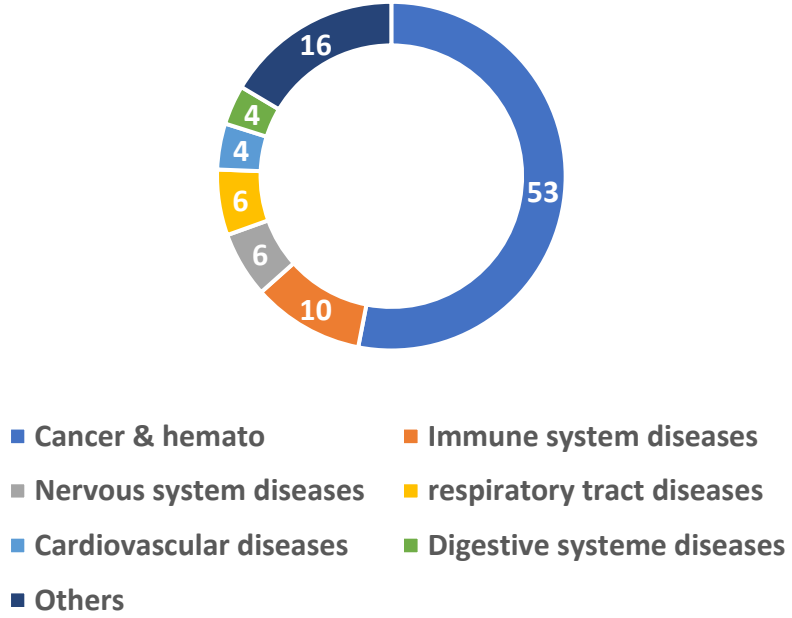
164 essais RIPH type 1 portant sur le médicament

Entre le 1er janvier 2022 et le 31 janvier 2023

Distribution par phase (%)



Distribution par aire thérapeutique (%)



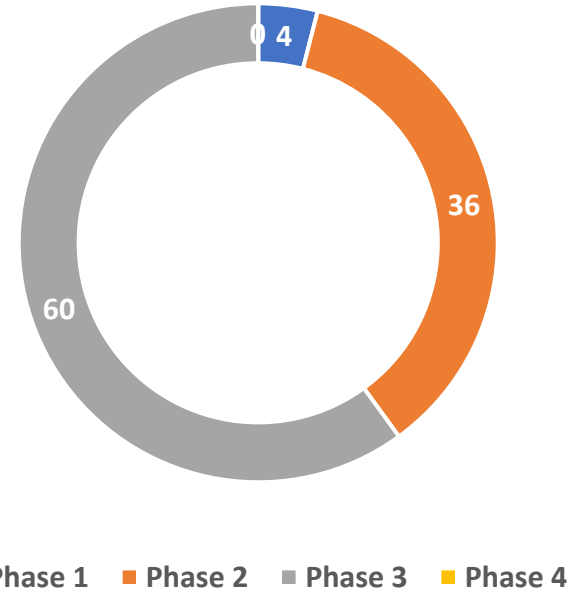
Caractérisation de l'échantillon issu de la base du Leem « OSCAR »
Volet « autorisation »: sous-échantillon dit « EU CTR »

Dépôt dans CTIS

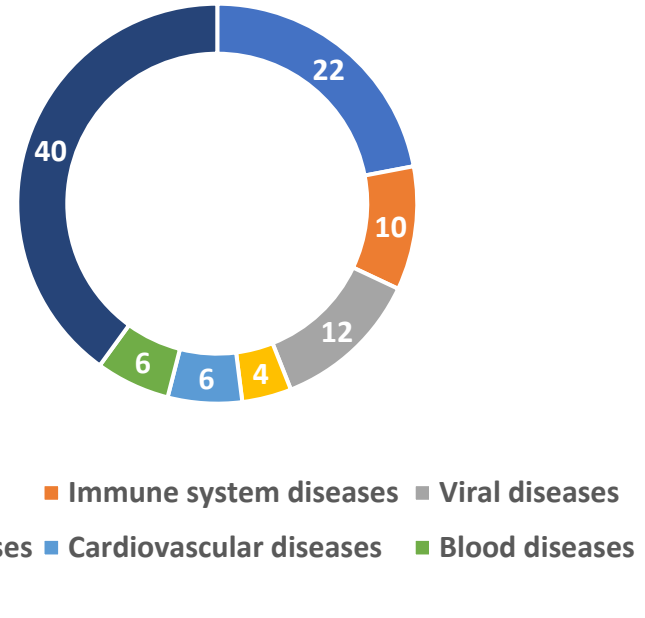
50 essais sur le médicament

Entre le 31 janvier 2022 et le 30 juin 2023

Distribution par phase (%)

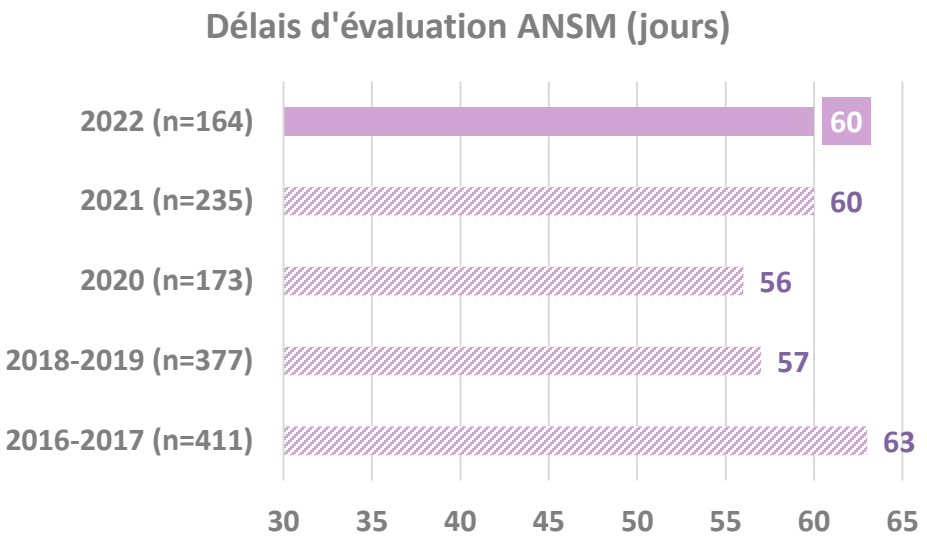


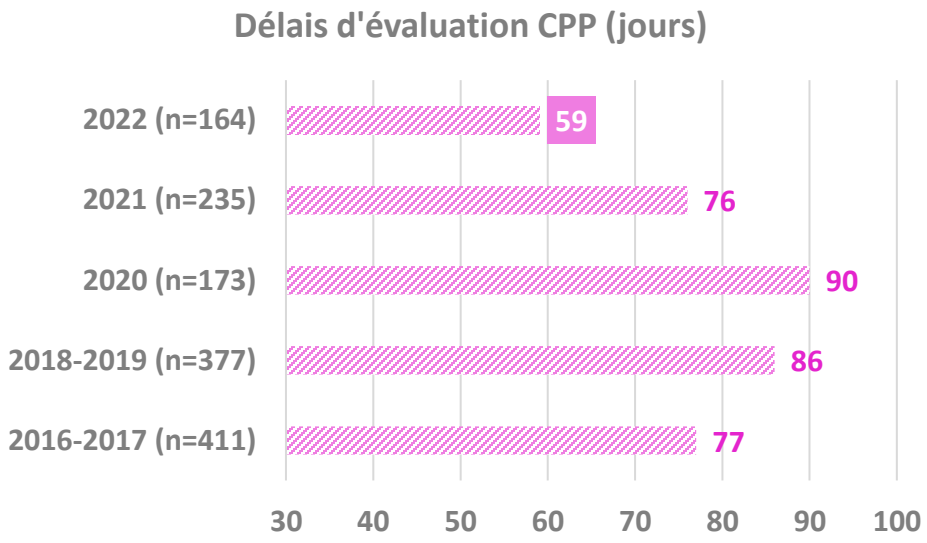
Distribution par aire thérapeutique (%)



Les délais d'évaluation par l'ANSM restent attractifs et ceux des CPP diminuent y compris pour l'oncologie et les maladies rares

Sous-échantillon « Loi Jardé »





Les délais médians d'évaluation sont de **60 jours pour l'ANSM** et de **59 jours pour les CPP**

En oncologie, ils sont de **57 jours** et **56 jours**, respectivement

Dans les maladies rares, **chacune des deux évaluations sont réalisées en 58 jours**

Focus sur la procédure de l'évaluation pour l'autorisation des essais cliniques

Sous-échantillon « Loi Jardé »

Nombre d'essais cliniques	ANSM	CPP
Evaluation sans question	20	2
Evaluation avec questions	144	162
Procédure de recours	NA	8

L'évaluation par l'ANSM a intégré une étape de questions-réponses avec le *sponsor* dans **88 %** des cas

L'évaluation par les CPP a intégré une étape de questions-réponses avec le *sponsor* dans **99 %** des cas

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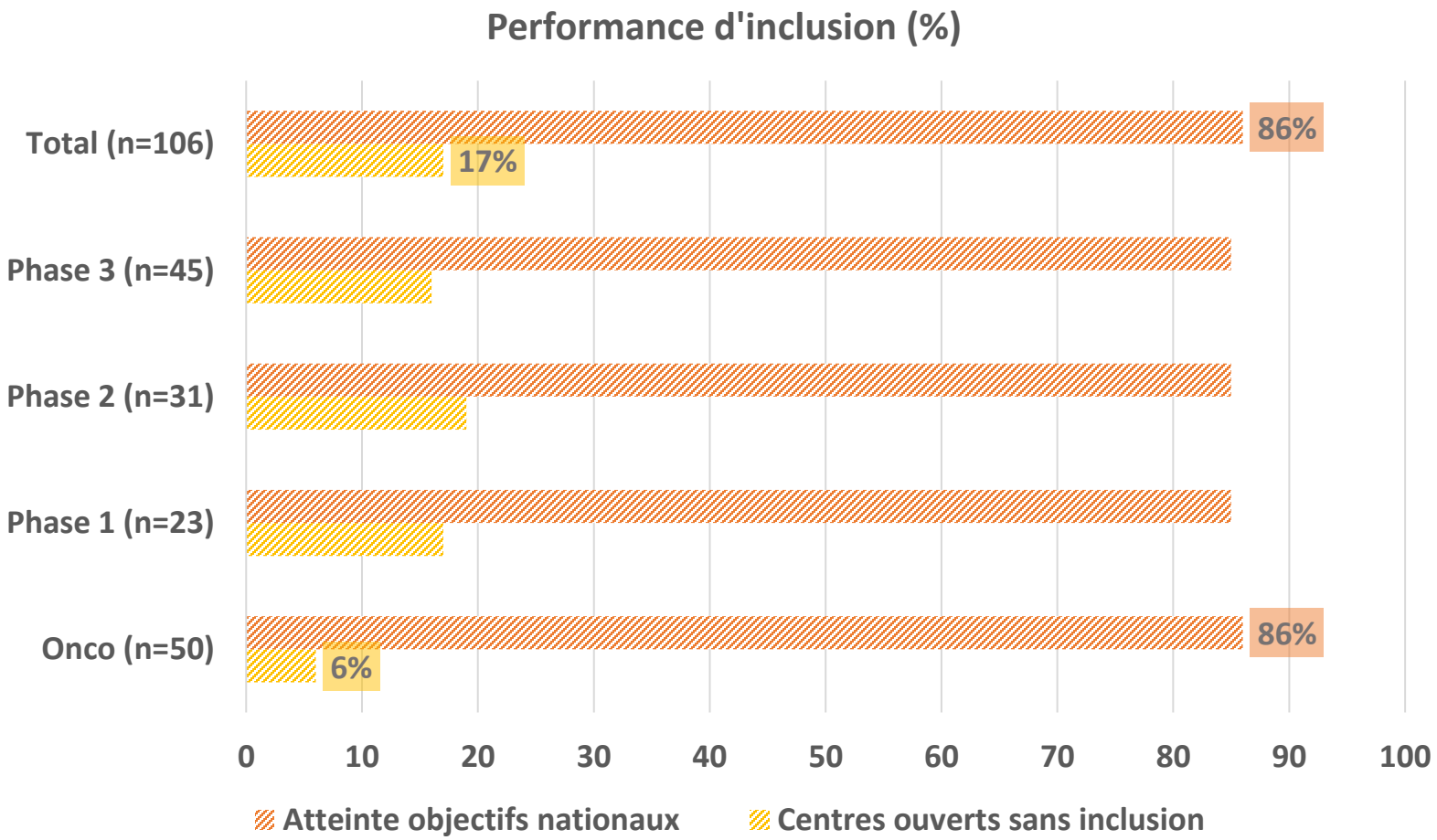
Les délais d'autorisation ont diminué mais les délais de contractualisation restent supra-réglementaires

Sous-échantillon « Loi Jardé »

Délais médians	2021	2022
ANSM	60 jours	60 jours
CPP	75 jours	59 jours
Convention unique	82 jours	79 jours

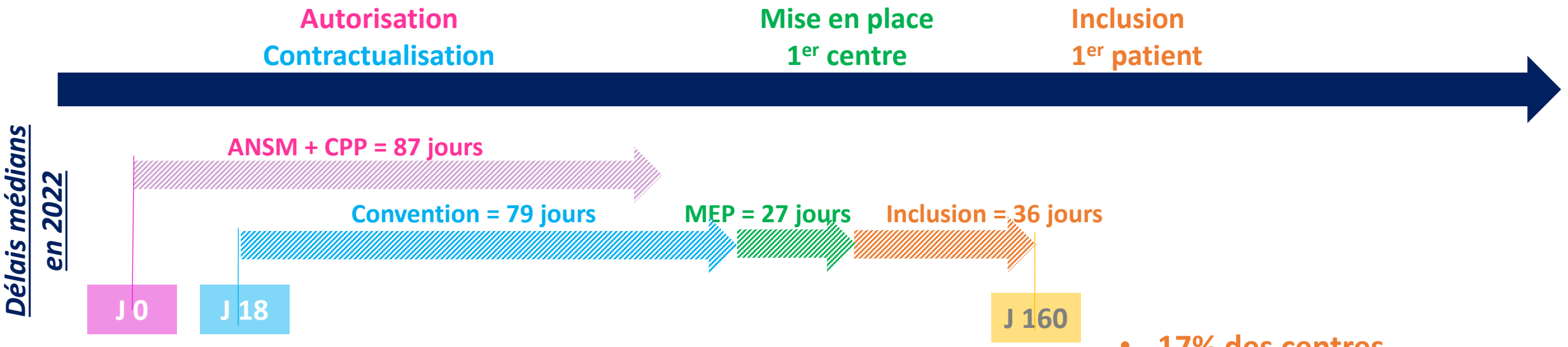
86% des objectifs nationaux d'inclusions ont été atteints et 17% des centres investigateurs sont restés inactifs

94% des objectifs d'inclusion sont atteints en Espagne



En 2022, 160 jours étaient nécessaires pour inclure un 1er patient en France

→ *les délais de démarrage doivent désormais composer avec les Règlements européens (CTR & IVDR) et les performances d'inclusion restent perfectibles*



- **17% des centres investigateurs sans inclusion**
- **86% des objectifs d'inclusion atteints**

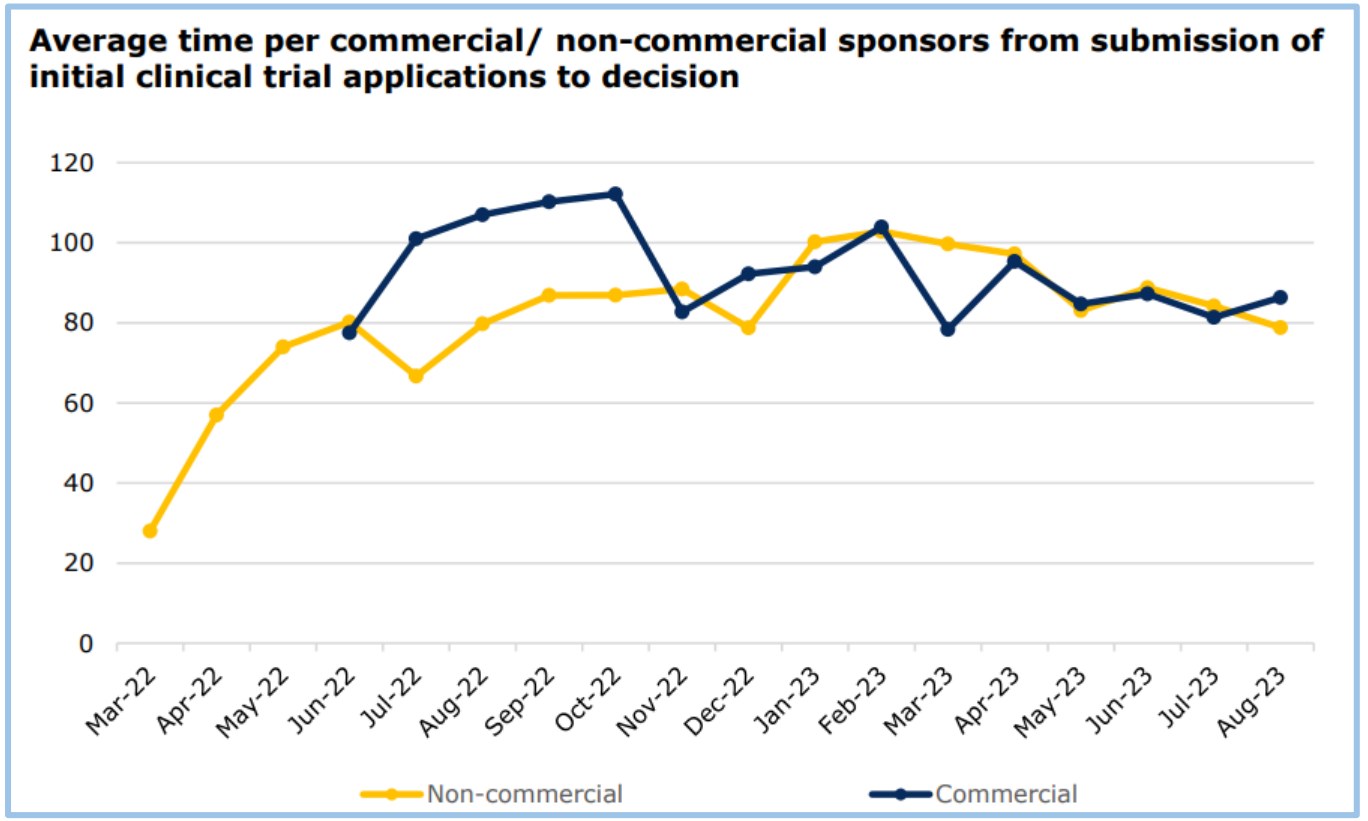
Premiers retours sur le EU CTR et sur l'utilisation du portail CTIS

Chiffres clés EMA (31/01/2022-31/08/2023) :

- *1 698 soumissions et 827 autorisations*
- *383 essais industriels multinationaux*
- *174 essais industriels mononationaux*

Activité de la France :

- *156 essais mononationaux (1er rang)*
- *416 essais multinationaux (3ème rang)*
- *Etat membre rapporteur pour 67 essais (3ème rang)*



Sous-échantillon « EU CTR »

Autorisation directe dans 81% seulement des cas (refus ou autorisation sous condition)

185 jours nécessaires pour inclure un 1er patient en France pour les essais déposés dans le portail CTIS

Premiers retours sur le EU CTR et sur l'utilisation du portail CTIS

N=50 essais	Dossiers recevables	Questions partie I	Questions partie II	Autorisation	EMR France
% oui	55	86	89	85	9
% non	45	14	4	15	91

La pratique devrait permettre une réduction du taux de dossiers irrecevables

Délais médians (en jours)	Autorisation	Contractualisation centre coordonnateur	Mise en place	Inclusion
En 2023	118 j	94 j	34 j	33 j

La pratique devrait permettre une réduction des délais d'autorisation

La contractualisation est le levier principal pour accélérer le démarrage des essais

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