

CJC-1295 with DAC

A prolonged growth-hormone-releasing hormone
analogue

Author

Valentine Wibowo, Clinical Researcher

Medical review

dr. I Wayan Cahyadi Surya Distira Putra, MPH

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ABSTRACT

DAC-mediated albumin association converts a short hypothalamic releasing signal into multi-day pituitary stimulation while retaining detectable pulsatility.

This monograph is restricted to CJC-1295 containing the drug-affinity complex (DAC). It does not discuss a no-DAC construct as though it were the same molecule and does not discuss a CJC-1295 plus ipamorelin mixture or laboratory cocktail.

This monograph begins with the molecule and follows the causal chain through biochemistry, cellular mechanism, exposure and integrated physiology. Population studies enter only at the terminal stress-test: useful for the proposition actually tested, incapable of defining the molecule or replacing the causal model.

ESTABLISHED	UNRESOLVED
• DAC construct defined • Albumin binding • Human GH/IGF-1 pharmacodynamics	• Patient-relevant efficacy • Long-term metabolic consequences • Outcome-specific dose architecture

EVIDENCE HIERARCHY

Mechanistic evidence is not a lower-grade substitute for population medicine. Physical constraints, biochemical measurements, historical and non-English records, exposure studies and clinical outcomes answer different questions. Controlled clinical trials test the complete implemented proposition; they cannot manufacture a missing identity, mechanism or exposure bridge.

I	Molecular identity and chemistry
II	Biochemistry and target architecture
III	Cells and ex-vivo tissues
IV	Animal and in-vivo pharmacology
V	Integrated physiology and translation
VI	Human PK and observational signal
VII	Controlled clinical trials

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ACTION LEDGER

Describe the action before judging its value.

Benefit is a downstream clinical judgement. The scientific object is the action itself: what moves, under which exposure, in which biological state, and where the inference stops.

01 Attributed biochemical action	DAC-mediated albumin association converts a short hypothalamic releasing signal into multi-day pituitary stimulation while retaining detectable pulsatility.
02 Exposure and reachability	Randomised ascending-dose studies in healthy adults estimated a half-life of approximately 5.8-8.1 days. A single injection increased mean GH for at least six days and IGF-1 for approximately nine to eleven days.
03 Physiological direction is contextual	Prolonged GHRH-receptor stimulation changes a regulated endocrine axis rather than supplying a simple replacement signal. Pulsatility, hepatic IGF-1 production, glucose handling, fluid balance, sleep-disordered breathing and negative feedback determine the organismal consequence. An IGF-1 rise establishes axis engagement; it does not, by itself, establish repair or favourable body composition.
04 Individual adjudication boundary	The path from sustained GH/IGF-1 movement to net benefit rather than glycaemic, fluid-retention or proliferative cost. A rise in GH or IGF-1 is proof of target engagement, not proof of recovery, body recomposition, sleep improvement or longevity.

METHODS AND COVERAGE

A reproducible boundary, not an implied exhaustive review.

This curated mechanistic monograph uses primary indexed records and reference-chaining. It does not claim systematic-review completeness. Absence of a retrieved result is not evidence that an effect is absent.

SEARCH SURFACE	PubMed/MEDLINE primary records, Russian-language indexed abstracts, and reference-chaining for entity-defining, historical and translational studies. Language, geography, regulatory status and journal fashion are not evidence grades.
QUERY FRAME	CJC-1295 with DAC · drug affinity complex · GHRH receptor · growth hormone · IGF-1 · albumin binding
EVIDENCE CUTOFF	23 August 2026
ENTITY EXCLUSION	CJC-1295 with DAC is distinct from a no-DAC GRF analogue and from every combination product. The albumin-reactive moiety is part of the pharmacological identity. Nomenclature must therefore preserve both the releasing-hormone analogue and the affinity complex: omitting DAC collapses two different concentration-time experiments into one name and makes downstream attribution scientifically unstable.
TRACEABILITY	10 extended claim units plus 2 historical records and 3 mechanistic-calculus records; 4 cited records in the complete corpus.
INTERPRETIVE RULE	Identity → physical constraint → measured reaction or binding → reachable exposure → system response → outcome. Statistical significance does not manufacture mechanism; mechanistic plausibility does not manufacture a patient outcome.

EVIDENCE ATLAS

Every claim keeps its experimental address.

10 claim units are mapped to evidentiary layer, experimental frame and source records. The layer describes the question answered; it is not a popularity score.

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
IMolecular identity	Entity resolution and albumin affinity · claim 1	CJC-1295 with DAC is a tetrasubstituted GRF(1-29) analogue carrying a reactive drug-affinity complex. Covalent binding to albumin is not a cosmetic modification: it transforms residence time and makes the DAC construct a different pharmacological entity from shorter-acting GRF analogues sold under similar names.	[1][3]
IMolecular identity	Entity resolution and albumin affinity · claim 2	Evidence attribution begins with the construct used in the human studies. The prolonged half-life, multi-day GH elevation and sustained IGF-1 response belong to CJC-1295 with DAC. They cannot be inherited by a no-DAC peptide and cannot be extrapolated to a combination product.	[1][2]
IVIntegrated in-vivo model	Pituitary mechanism and endocrine dynamics · claim 1	The peptide activates the growth-hormone-releasing hormone receptor on pituitary somatotrophs. This increases endogenous GH secretion and downstream hepatic and tissue IGF-1 signalling. The biological programme remains mediated by an intact hypothalamic-pituitary axis rather than by administration of exogenous GH itself.	[1][2]
VIHuman exposure or signal	Pituitary mechanism and endocrine dynamics · claim 2	Pulsatility was reported to remain detectable despite prolonged exposure. That observation is mechanistically important, but preservation of pulses does not prove physiological equivalence. Pulse amplitude, integrated exposure, feedback, sleep, glucose and baseline endocrine state can all change the downstream phenotype.	[1][2]
VIHuman exposure or signal	Human pharmacokinetics and target engagement · claim 1	Ascending-dose studies in healthy adults estimated an apparent half-life of approximately 5.8 to 8.1 days. A single subcutaneous injection increased mean GH for at least six days and IGF-1 for approximately nine to eleven days; repeated administration produced cumulative IGF-1 elevation.	[1]

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
VI Human exposure or signal	Human pharmacokinetics and target engagement · claim 2	These findings establish exposure and endocrine target engagement. They do not establish improvement in sleep, recovery, body composition, cognition or longevity. GH and IGF-1 are intermediate biological signals whose relationship with benefit and harm depends on age, metabolic state, tissue sensitivity and duration.	[1][4]
IV Integrated in-vivo model	Proteomic response and interpretation · claim 1	A small proteomic study examined sera from eleven healthy young men before and one week after CJC-1295. Several protein spots changed, including apolipoprotein A1 and transthyretin isoforms. This demonstrates downstream biological perturbation but does not establish clinical utility or a validated response biomarker.	[4]
IV Integrated in-vivo model	Proteomic response and interpretation · claim 2	The proteomic observations illustrate why a rise in IGF-1 should not be treated as the whole mechanism. Growth signalling reorganises multiple protein and tissue processes. The direction and clinical meaning of that reorganisation require outcome-specific study.	[4]
IV Integrated in-vivo model	Boundaries of clinical inference · claim 1	Potential boundaries arise from the same axis that creates the desired pharmacology: oedema, paraesthesia, arthralgia, worsening glucose regulation, sleep-apnoea context and proliferative signalling. These are mechanistic monitoring domains, not proof that harm will occur in every exposed person.	[1][4]
VI Human exposure or signal	Boundaries of clinical inference · claim 2	The human programme is strong for identity, exposure and GH/IGF-1 pharmacodynamics but thin for patient-important outcomes. Any proposition beyond target engagement therefore requires a defined phenotype, comparator, functional endpoint and stopping rule rather than a generic optimisation narrative.	[1][2][4]

SECTION 01

Molecular dossier: the entity before the outcome

ENTITY — Tetrasubstituted GRF(1-29) analogue bearing a drug-affinity complex

BIOCHEMICAL CLASS — Albumin-binding GHRH-receptor agonist

PRIMARY SYSTEM — GHRHR → pulsatile GH → IGF-1 axis

IDENTITY BOUNDARY — CJC-1295 with DAC is distinct from a no-DAC GRF analogue and from every combination product. The albumin-reactive moiety is part of the pharmacological identity. Nomenclature must therefore preserve both the releasing-hormone analogue and the affinity complex: omitting DAC collapses two different concentration-time experiments into one name and makes downstream attribution scientifically unstable.

SECTION 02

Historical and international corpus

CJC-1295 with DAC is a 2000s engineered entity derived from older GHRH physiology. Only the DAC construct owns the multi-day pharmacokinetic and endocrine observations.

The literature is strong for construct identity, albumin binding, exposure and GH/IGF-1 target engagement, but thin for patient-important outcomes.

SECTION 03

GHRH lineage: Older endocrine physiology defines the axis, not the product

Hypothalamic-pituitary GH physiology predates CJC-1295. The drug-affinity complex changes residence time so profoundly that earlier short GHRH fragments cannot supply its exposure assumptions.[2][3]

SECTION 04

2005-2009: Compact but direct construct-specific programme

The defining publications established albumin-linked persistence, multi-day hormone responses and downstream serum-protein perturbation. A small corpus can be mechanistically powerful when it directly resolves identity and exposure.[1][2][3][4]

SECTION 05

Mechanistic calculus — CONSTRAINED: DAC changes the pharmacological entity

Covalent albumin association alters effective molecular size, clearance and concentration-time behaviour. A no-DAC peptide cannot inherit the reported half-life by nomenclature.[1][3]

SECTION 06

Mechanistic calculus — MEASURED: Exposure and endocrine response occupy different clocks

The reported apparent half-life was approximately 5.8-8.1 days; GH and IGF-1 responses persisted on different multi-day intervals. These clocks must be modelled separately rather than called a single duration of action.[1]

SECTION 07

Mechanistic calculus — UNRESOLVED: Endocrine engagement is not an outcome function

No equation converts a given GH or IGF-1 increment into recovery, sleep, body composition or longevity. Feedback, age, glucose state and tissue sensitivity leave that mapping unresolved.[1][4]

SECTION 08

Causal architecture: DAC changes molecular residence

The reactive affinity complex binds circulating albumin and protects the GRF analogue from the rapid clearance expected of the unmodified releasing fragment. This modification creates the multi-day exposure profile and makes no-DAC material a different pharmacological entity.[1][3]

SECTION 09

Causal architecture: Pituitary stimulation remains upstream

GHRHR activation on somatotrophs increases endogenous GH release rather than supplying exogenous GH. Hypothalamic-pituitary feedback, baseline reserve, sleep and metabolic state therefore remain within the causal system.[1][2]

SECTION 10

Causal architecture: IGF-1 is a downstream mediator and boundary

GH changes hepatic and tissue IGF-1 signalling, substrate handling, fluid balance and protein turnover. Those pathways can support anabolism while also creating glycaemic and proliferative tensions. Direction of biomarker movement alone cannot settle the net organismal effect.[1][4]

SECTION 11

Causal architecture: Pulsatility is not physiological equivalence

Detectable GH pulses during prolonged stimulation are mechanistically relevant, yet pulse amplitude, integrated exposure and feedback can differ from baseline physiology. Preserved temporal structure must not be used to claim restored endocrine homeostasis without direct measurement.[1][2]

SECTION 12

Molecular identity and entity resolution

Here CJC-1295 means the DAC construct: a tetrasubstituted GRF(1-29) analogue bearing a drug-affinity complex that binds albumin. A shorter-acting no-DAC construct is a different entity and cannot inherit its pharmacokinetics.

SECTION 13

Biochemical mechanism and target architecture

CJC-1295 with DAC engages the GHRH receptor and prolongs stimulation of pulsatile growth-hormone secretion, with downstream IGF-1 elevation. Target engagement does not itself establish recovery, body-composition, sleep or longevity benefit.

SECTION 14

In-vivo pharmacology and exposure

Randomised ascending-dose studies in healthy adults estimated a half-life of approximately 5.8-8.1 days. A single injection increased mean GH for at least six days and IGF-1 for approximately nine to eleven days.

SECTION 15

Integrated physiology and individual terrain

Prolonged GHRH-receptor stimulation changes a regulated endocrine axis rather than supplying a simple replacement signal. Pulsatility, hepatic IGF-1 production, glucose handling, fluid balance, sleep-disordered breathing and negative feedback determine the organismal consequence. An IGF-1 rise establishes axis engagement; it does not, by itself, establish repair or favourable body composition.

SECTION 16

Terminal human stress-test

Human studies establish prolonged GH-axis engagement and preservation of pulsatility. They do not establish patient-relevant outcomes in recovery, body composition or healthy ageing.

SECTION 17

Counterevidence and causal boundaries

An IGF-1 rise is a pharmacodynamic signal, not a clinical success. Oedema, paraesthesia, arthralgia, glycaemic deterioration, sleep-apnoea context and growth signalling remain biologically relevant boundaries.

SECTION 18

Scientific conclusion

CJC-1295 with DAC has defined identity and credible human pharmacodynamics. Clinical claims must remain narrower than verified GH/IGF-1 target engagement and must never be transferred to a no-DAC construct.

SECTION 19

Entity resolution and albumin affinity

CJC-1295 with DAC is a tetrasubstituted GRF(1-29) analogue carrying a reactive drug-affinity complex. Covalent binding to albumin is not a cosmetic modification: it transforms residence time and makes the DAC construct a different pharmacological entity from shorter-acting GRF analogues sold under similar names.[1][3]

Evidence attribution begins with the construct used in the human studies. The prolonged half-life, multi-day GH elevation and sustained IGF-1 response belong to CJC-1295 with DAC. They cannot be inherited by a no-DAC peptide and cannot be extrapolated to a combination product.[1][2]

SECTION 20

Pituitary mechanism and endocrine dynamics

The peptide activates the growth-hormone-releasing hormone receptor on pituitary somatotrophs. This increases endogenous GH secretion and downstream hepatic and tissue IGF-1 signalling. The biological programme remains mediated by an intact hypothalamic-pituitary axis rather than by administration of exogenous GH itself.[1][2]

Pulsatility was reported to remain detectable despite prolonged exposure. That observation is mechanistically important, but preservation of pulses does not prove physiological equivalence. Pulse amplitude, integrated exposure, feedback, sleep, glucose and baseline endocrine state can all change the downstream phenotype.[1][2]

SECTION 21

Human pharmacokinetics and target engagement

Ascending-dose studies in healthy adults estimated an apparent half-life of approximately 5.8 to 8.1 days. A single subcutaneous injection increased mean GH for at least six days and IGF-1 for approximately nine to eleven days; repeated administration produced cumulative IGF-1 elevation.[1]

These findings establish exposure and endocrine target engagement. They do not establish improvement in sleep, recovery, body composition, cognition or longevity. GH and IGF-1 are intermediate biological signals whose relationship with benefit and harm depends on age, metabolic state, tissue sensitivity and duration.[1][4]

SECTION 22

Proteomic response and interpretation

A small proteomic study examined sera from eleven healthy young men before and one week after CJC-1295. Several protein spots changed, including apolipoprotein A1 and transthyretin isoforms. This demonstrates downstream biological perturbation but does not establish clinical utility or a validated response biomarker.[4]

The proteomic observations illustrate why a rise in IGF-1 should not be treated as the whole mechanism. Growth signalling reorganises multiple protein and tissue processes. The direction and clinical meaning of that reorganisation require outcome-specific study.[4]

SECTION 23

Boundaries of clinical inference

Potential boundaries arise from the same axis that creates the desired pharmacology: oedema, paraesthesia, arthralgia, worsening glucose regulation, sleep-apnoea context and proliferative signalling. These are mechanistic monitoring domains, not proof that harm will occur in every exposed person.[1][4]

The human programme is strong for identity, exposure and GH/IGF-1 pharmacodynamics but thin for patient-important outcomes. Any proposition beyond target engagement therefore requires a defined phenotype, comparator, functional endpoint and stopping rule rather than a generic optimisation narrative.[1][2][4]

SECTION 24

Falsification map

Failure of albumin association or multi-day exposure would invalidate DAC-based attribution.

IGF-1 elevation without a prespecified functional benefit would refute biomarker-as-benefit reasoning.

Deteriorating glucose, oedema or sleep-disordered breathing would falsify a net-benefit claim for that phenotype.

RESEARCH AGENDA

What would materially change the conclusion?

01 Outcome-specific trials using the exact DAC construct

02 Longitudinal glucose and sleep-apnoea effects

03 Dose-exposure-response modelling beyond IGF-1

04 Body-composition and functional endpoints

05 Long-term feedback and endocrine recovery after discontinuation

CITED PRIMARY EVIDENCE CORPUS

4 source records

This corpus documents the claims made in this monograph; it is not presented as an exhaustive systematic-review search.

Teichman et al. J Clin Endocrinol Metab. 2006;91:799-805. · PMID 16352683

Jetté et al. Endocrinology. 2005;146:3052-3058. · PMID 15817669

Ionescu & Frohman. J Clin Endocrinol Metab. 2006;91:4792-4797. · PMID 17018654

Chung et al. Activation of the GH/IGF-1 axis by CJC-1295 results in serum protein profile changes. Growth Horm IGF Res. 2009. · PMID 19386527

AUTHORSHIP AND ACCOUNTABILITY

Valentine Wibowo performed the conceptualisation, evidence synthesis, scientific interpretation and drafting. dr. I Wayan Cahyadi Surya Distira Putra, MPH completed medical review and approved the publication. Internal medical review is not represented as independent journal peer review.

No new patient data or human research were undertaken. The author and reviewer declare no personal financial competing interests. Clinic Terrain and Klinik Pratama Cepat Sehat provide clinical services; that institutional relationship is disclosed.